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TRANSACTIONS

OF THE

PATHOLOGICAL SOCIETY OF LONDON.

VOLUME THE FORTY-THIRD.

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THE present publication, being the Forty-third Volume of Transactions, constitutes the Forty-sixth published Annual Report of the Pathological Society's Proceedings.

The COUNCIL think it right to repeat that the exhibitors are alone responsible for the descriptions given of the Specimens exhibited by them, the only change made in the Reports furnished by the authors being such verbal alterations as were absolutely necessary.

20, HANOVER SQUARE, W.;
October, 1892.

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Presidents of the Society.

ELECTED

1846 CHARLES J. B. WILLIAMS, M.D., F.R.S.
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OF THE

Pathological Society of London,

ELECTED AT

THE GENERAL MEETING, MAY 17TH, 1892,

FOR THE SESSION 1892–93.

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*** *Members are requested to inform the Secretaries of any corrections which may be necessary.*

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CHAUVEAU, A., M.D., Professor of Physiology at the Medical School of Lyons.
VON HELMHOLTZ, H., M.D., Professor of Physiology in the University of Heidelberg.
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PASTEUR, PROFESSOR L., Member of the Institute, Paris.
RINDFLEISCH, EDOUARD, M.D., Professor of Pathological Anatomy in the University of Bonn.
SIMON, SIR JOHN, K.C.B., D.C.L., LL.D., F.R.S., 40, Kensington-square, W.
THIERSCH, CARL, M.D., Professor of Surgery in the University of Leipzig.
VIRCHOW, RUDOLF, M.D., Professor of Pathological Anatomy in the University of Berlin.

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O.M.—Original Member.
Pres.—President.
T.—Treasurer.
V.-P.—Vice-President.
S.—Secretary.
C.—Member of Council.

Those marked thus (L) have paid Composition Fee for Annual Subscription.
Those marked thus (‡) have paid Composition Fee for Transactions.

GENERAL LIST OF MEMBERS.

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1891 ABBOTT, FRANCIS CHARLES, M.D., St. Thomas's Hospital Medical School, S.E.

L1879 ABERCROMBIE, JOHN, M.D., 23, Upper Wimpole-street, W.

1885 ABRAHAM, PHINEAS S., M.A., M.D., 2, Henrietta Street, W.

1858 ACLAND, Sir HENRY WENTWORTH, Bart., K.C.B., M.D., F.R.S., Broad-street, Oxford.

1883 ACLAND, THEODORE DYKE, M.D., 74, Brook-street, W. (C. 1892.)

1891 ADAMI, J. GEORGE, M.A., M.B., Jesus College, Cambridge.

‡1866 ADAMS, ARTHUR BAYLEY.

1890 ADAMS, JAMES, 4, Chiswick-place, Eastbourne.

LO.M. ADAMS, WILLIAM, 5, Henrietta-street, Cavendish-square, W. (C. 1851-4. V.-P. 1867-9.)

L1848 AIKIN, CHARLES A., 7, Clifton-place, Sussex-square, W. (C. 1864-6.)

1872 AIKIN, CHARLES EDMUND, 7, Clifton-place, Sussex-square, W.

1882 ALLCHIN, WILLIAM HENRY, M.B., 5, Chandos-street, W.

1877 ALTHAUS, JULIUS, M.D., 48, Harley-street, W.

1884 ANDERSON, ALEXANDER RICHARD, 5, East Circus-street, Nottingham.

1868 ANDERSON, J. FORD, M.D., 41, Belsize-park, N.W.

1880 ANDERSON, JAMES, M.A., M.D., C.M., 41, Wimpole-street, W.

1871 ANDERSON, WILLIAM, 2, Harley-street, W. (C. 1888-90.)

L1863 ANDREW, JAMES, M.D., 22, Harley-street, W. (C. 1868-70. V.-P. 1889-90.)

1887 ARKLE, CHARLES, M.D., 66, Wimpole-street, W.

1883 ASHBY, HENRY, M.D., 13, St. John-street, Manchester.

1882 AXE, J. WORTLEY, College House, Great College-street, N.W.

1863 BAGSHAWE, FREDERICK, M.A., M.D., 16, Warrior-square, Hastings.

‡1856 BALDING, DANIEL BARLEY, Royston, Herts.

1889 BALGARNIE, WILFRED, 47, South Molton-street, W.

1880 BALL, BENJAMIN, rue du Faubourg St. Honoré, 3, Paris.

1881 BALLANCE, CHARLES A., M.S., 56, Harley-street, W. (C. 1890-2.)

1875 BARKER, ARTHUR E. J., 87, Harley-street, W. (C. 1884-6.)

1885 BARLING, GILBERT, M.B., 85, Edmund-street, Birmingham.

1874 BARLOW, THOMAS, M.D., B.S., 10, Wimpole-street, W. (C. 1879-81.)

1862 BARRATT, JOSEPH GILLMAN, M.D.

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1881 BARRS, ALFRED GEORGE, M.D., 22, Park-place, Leeds.

1879 BARTLETT, HENRY, M.D., Defoe-road, Tooting-corner, S.W.

L1853 BARWELL, RICHARD, 55, Wimpole-street, W. (C. 1862-4. V.-P. 1889-90.)

Elected

L1861 BASTIAN, H. CHARLTON, M.A., M.D., F.R.S, 8A, Manchester-square, W. (C. 1869-71. V.-P. 1885-7.)

1877 BATEMAN, ARTHUR W., B.A., Tenterfield, New South Wales.

L1876 BATTESON, JOHN, 26, Windsor-road, Forest-gate, E.

1882 BATTLE, WILLIAM HENRY, 6, Harley-street, W.

1870 BÄUMLER, CHRISTIAN G. H., M.D., University of Erlangen.

1874 BEACH, FLETCHER, M.B., Metropolitan District Asylum, Darenth, near Dartford, Kent.

1879 BEALE, EDWIN CLIFFORD, M.B., 23, Upper Berkeley-street, W.

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1856 BEALEY, ADAM, M.D., M.A., Felsham Lodge, Hollington-park, St. Leonard's-on-Sea.

1870 BECK, MARCUS, M.S., 30, Wimpole-street, W. (C. 1875-7. V.-P. 1888-9.)

1865 BEEBY, WALTER, M.D., Bromley, Kent.

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1883 BENHAM, ROBERT FITZROY, Abercorn House, Castletown-road, West Kensington, W.

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L1850 BIRKETT, EDMUND LLOYD, M.D., Westbourne Rectory, Emsworth, Hampshire. (C. 1856-7.)

1881 BISS, CECIL YATES, M.D., 135, Harley-street, W.

1865 BISSHOPP, JAMES, Bedford-place, Tunbridge Wells.

1877 BLACK, JAMES, Hillside, Hermitage-road, Norwood.

1889 BLACK, ROBERT, M.D., 6, Pavilion Parade, Brighton.

1850 BLAGDEN, ROBERT, Stroud, Gloucestershire.

1863 BLANCHET, JEAN B., M.D., M.S., Montreal, Quebec, Canada.

1876 BLASSON, WILLIAM, Edgeware, Middlesex.

1879 BOILEAU, J. P. H., M.D., Brigade-Surgeon, Army.

1876 BOND, THOMAS, M.B., 7, Broad Sanctuary, Westminster, S.W.

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1881 BOWLBY, ANTHONY A., 24, Manchester-square, W. (C. 1886-8.)

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1882 Boyd, Stanley, M.B., 134, Harley-street, W.
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1883 Bradshaw, James Dixon, M.B., 30, George-street, Hanover-square, W.
1880 Bramwell, Byrom, M.D., 23, Drumsheugh-gardens West, Edinburgh.
1889 Bredin, J. Noble, 1, Norton Folgate, E.
1877 Bridges, Robert, M.B., M.A., Manor House, Yattendon, Berks.
‡1867 Bridgewater, Thomas, LL.D. Glas., M.B. Lond., Harrow-on-the-Hill, Middlesex.
1873 Briggs, Jacob Myers, M.D., Coeymans, New York, U.S.
1868 Bright, George Charles, M.D., Cannes, Alpes Maritimes, France.
1857 Briscoe, John, 12, Broad-street, Oxford.
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L1851 Bristowe, John S., M.D., F.R.S., 13, Old Burlington-street, W. (C. 1854-8. S. 1861-4. C. 1865-7. V.-P. 1868-76, 1887. P. 1885-6.)
1860 Broadbent, William Henry, M.D., 84, Brook-street, W. (C. 1871-3. V.P. 1882-4.)
1886 Brockatt, Andrew Alexander, St. Cuthbert's, Malvern.
L1852 Brodhurst, Bernard E., 20, Grosvenor-street, W. (C. 1862-4.)
1884 Brodie, Charles Gordon, 30, Harley-street, W.
1863 Brodie, George Bernard, M.D., 3, Chesterfield-street, Mayfair, W.
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1875 Browne, George Buckston, 80, Wimpole-street, Cavendish-square, W.
L1866 Browne, Lennox, 15, Mansfield-street, W.
1877 Bruce, J. Mitchell, M.D., 70, Harley-street, W.
1890 Brunton, T. Lauder, M.D., D.Sc., LL.D., F.R.S., 10, Stratford-place, W.
L1855 Bryant, Thomas, 65, Grosvenor-street, W. (C. 1863-6. V.-P. 1877-9.)
L1854 Buchanan, George, M.D., F.R.S., 27, Woburn-square, W.C. (C. 1864-6. V.-P. 1880-2.)
1890 Buckland, Francis O., M.A., M.B., C.M., 6, Lower Sloane-street, S.W.
1891 Burghard, Frederic Francois, M.D., M.S., 46, Weymouth-street, W.
1878 Burnet, Robert William, M.D., 6, Upper Wimpole-street, W.
1880 Burton, Samuel Herbert, M.B., Norfolk and Norwich Hospital, Norwich.
1887 Butler-Smythe, Albert Charles, 76, Brook-street, W.
1872 Butlin, Henry Trentham (C.), 82, Harley-street, W. (C. 1876-8, 1887-9. S. 1884-6. V.-P. 1891-2.)
1866 Butt, William Frederick.
1883 Buxton, Dudley W., M.D., 82, Mortimer-street, W.
1856 Buzzard, Thomas, M.D., 74, Grosvenor-street, W. (C. 1869-70. V.-P. 1881-3.)

1885 Cahill, John, 12, Seville-street, Lowndes-square, S.W.
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1864 CAY, CHARLES VIDLER, Deputy Surgeon-General, Army.
1863 CAYLEY, WILLIAM, M.D. (TREASURER), 27, Wimpole-street, W. (C. 1870-1, 1875-8. S. 1872-4. V.-P. 1884-6. T. 1888-92.)
1869 CHAFFERS, EDWARD, Keighley, Yorkshire.
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1891 CHAPLIN, ARNOLD, M.B., City of London Hospital for Diseases of the Chest, Victoria Park, N.E.
1876 CHARLES, T. CRANSTOUN, M.D., M.C., Albert Mansions, 106, Victoria-street, Westminster, S.W.
1884 CHAVASSE, THOMAS FREDERICK, M.D., C.M., 24, Temple-row, Birmingham.
1879 CHEYNE, WILLIAM WATSON, M.B., C.M., 59, Welbeck-street, W. (C. 1885-7. V.-P. 1892.)
1858 CHILD, GILBERT W., Cowley House, Oxford.
1873 CHISHOLM, EDWIN, M.D., Abergeldie, Ashfield, near Sydney, New South Wales [care of Messrs. Dawson, 121, Cannon-street, E.C.].
1865 CHURCH, WILLIAM SELBY, M.D., 130, Harley-street, W. (C. 1871-3.)
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1872 CLARK, ANDREW, 71, Harley-street, W.
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L1875 CLUTTON, HENRY HUGH, M.A., 2, Portland-place, W. (C. 1884-6. V.-P. 1892.)
‡1865 COATES, CHARLES, M.D., 10, Circus, Bath.
1885 COATS, JOSEPH, M.D., 31, Lynedoch-street, Glasgow.
1856 COCKLE, JOHN, M.D., M.A., 5, Suffolk-place, S.W.
1886 COLLIER, WILLIAM, M.D., 62, High-street, Oxford.
1891 COLLINS, EDWARD TREACHER, 47, Devonshire-street, W.
1888 COLLINS, WILLIAM JOB, M.D., M.S., 1, Albert-terrace, Regent's-park, N.W.
1878 COLLYNS, R. T. POOLE, 20, Lingfield-road, Wimbledon.
1888 COLMAN, WALTER STACY, M.B., 41, Torrington-square, W.C.

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1882 COLQUHOUN, DANIEL, M.D., Dunedin, New Zealand.
1891 COOK, HERBERT G. GRAHAM, Victoria Hospital, Chelsea, S.W.
1858 COOKE, R. T. E. BARRINGTON, 15, St. Nicholas-cliff, Scarborough, Yorkshire.
1871 COOKE, THOMAS, 40, Brunswick-square, W.C.
1866 COOMBS, ROWLAND HILL, Mill-street, Bedford.
1892 COOPER, C. DUDLEY, 171, Stanhope-street, N.W.
1889 COPEMAN, SYDNEY ARTHUR MONCKTON, M.A., M.D., Local Government Board, Whitehall, S.W.
1875 CORY, ROBERT, M.D., 73, Lambeth Palace-road, S.E.
1892 COTTERELL, EDWARD, 5, Halkin-street West, S.W.
1876 COTTLE, WYNDHAM, M.D., 3, Savile-row, W.
L1861 COUPER, JOHN, 80, Grosvenor-street, W. (C. 1870-2.)
1873 COUPLAND, SIDNEY, M.D., 16, Queen Anne-street, W. (C. 1878-81, 1889-91. S. 1886-8. V.-P. 1892.)
1884 CRICHTON, GEORGE, M.B., 3, Cambridge-villas, Twickenham.
1873 CRIPPS, WILLIAM HARRISON, 2, Stratford-place, W. (C. 1883-5.)
1877 CROCKER, HENRY RADCLIFFE, M.D., 121, Harley-street, W. (C. 1887-9.)
1856 CROFT, JOHN, 3, Mansfield-street, W. (C. 1870-2. V.-P. 1882-4.)
1879 CROOKE, GEORGE FREDERICK, M.D., 2, Edmund-street, Birmingham.
1886 CROOKSHANK, EDGAR, M.B., Saint Hill, near East Grinstead, Sussex. (C. 1890-2.)
1861 CROSBY, THOMAS BOOR, M.D., 21, Gordon-square, W.C.
1875 CROSS, FRANCIS RICHARDSON, 5, The Mall, Clifton, Bristol.
1890 CROWLE, THOMAS H. RICKARD, 3, Campden Hill-road, W.
1889 CUFF, ROBERT, M.B., Huntriss-row, Scarborough.
1885 CULLINGWORTH, CHARLES JAMES, M.D., 46, Brook-street, W.
1871 CUMBERBATCH, ELKIN, 17, Queen Anne-street, W.
1873 CURNOW, JOHN, M.D., 3, George-street, Hanover-square, W. (C. 1882-4.)

1884 DAKIN, W. RADFORD, M.D., B.S., 57, Welbeck-street, W.
1884 DALLAWAY, DENNIS, 5, Duchess-street, W.
1883 DALTON, NORMAN, M.D., 4, Mansfield-street, W.
1873 DAVIDSON, ALEXANDER, M.D., 2, Gambier-terrace, Liverpool.
1885 DAVIES, ARTHUR, M.D., 23, Finsbury-square, E.C.
L1869 DAVIES-COLLEY, J. NEVILLE C., M.B., 36, Harley-street, W. (C. 1880-2. V.-P. 1890-1.)
1883 DAVIS, EDWIN HARRY, West Hartlepool.
‡1859 DAVIS, FRANCIS WILLIAM, R.N. [Agents: Messrs. Hallett and Co., 7, St. Martin's-place, Trafalgar-square, W.C.]
1879 DAVY, HENRY, M.D., 29, Southernhay, Exeter.
1866 DAY, WILLIAM HENRY, M.D., 10, Manchester-square, W.
1889 DEAN, HENRY PERCY, M.B., B.S., 84, Wimpole-street, W.
1887 DELÉPINE, SHERIDAN, M.B., 258, Oxford-road, Manchester.
1880 DENT, CLINTON T., 61, Brook-street, W.

Elected

1856 Dick, H., M.D.

1871 Dickinson, Edward Harriman, M.A., M.D., 162, Bedford-street, Liverpool.

L1858 Dickinson, William Howship, M.D., 9, Chesterfield-street, W. (C. 1866-8. S. 1869-71. V.-P. 1872-4. P. 1889-90.)

L1890 Dickinson, William Lee, M.B., 9, Chesterfield-street, W.

1872 Diver, Ebenezer, M.D., Kenley, Caterham-valley, Surrey.

1872 Doran, Alban Henry Griffiths, 9, Granville-place, W. (C. 1882-4.)

L1866 Down, John Langdon H., M.D., 81, Harley-street, W. (C. 1872-4.)

1877 Drake-Brockman, E. F., Madras Medical Service [care of Mr. Lewis, Gower-street, W.C.].

1880 Dreschfeld, Julius, M.D., 325, Oxford-road, Manchester.

1879 Drewitt, F. G. Dawtrey, M.D., 2, Manchester-square, W. (C. 1890-2.)

L1865 Duckworth, Sir Dyce, M.D., LL.D., 11, Grafton-street, Bond-street, W. (C. 1877.)

L1847 Dudgeon, Robert E., M.D., 53, Montagu-square, W.

1865 Duffin, Alfred Baynard, M.D., 18, Devonshire-street, Portland-place, W. (C. 1872-4.)

1868 Duke, Oliver Thomas, M.B., India.

1871 Dukes, Clement, M.D., B.S., Sunnyside, Rugby.

1877 Dunbar, J. J. MacWhirter, M.D., Hedingham House, Clapham-common, S.W.

1877 Duncan, Andrew, M.D., 8, Henrietta-street, Covent-garden, W.C.

1889 Duncan, John, M.D., St. Petersburg.

1884 Dunn, Louis Albert, M.B., M.S., 10, St. Thomas's-street, S.E.

1858 Durham, Arthur Edward, 82, Brook-street, W. (C. 1869-71. V.P. 1883-5.)

1879 Durham, Frederic, M.B., 82, Brook-street, W.

L1880 Edmunds, Walter, M.C., 75, Lambeth Palace-road, S.E. (C. 1892.)

1882 Edwards, F. Swinford, 55, Harley-street, W.

1889 Elam, William Henry, New Barnet, Herts.

1883 Elder, George, M.D., 17, Regent-street, Nottingham.

1867 Ellis, James, M.D., California.

1873 Engelmann, George Julius, M.D., A.M., 3003, Locust-street, St. Louis, Miss., U.S.

L1846 Erichsen, John Eric, LL.D., F.R.S., 6, Cavendish-place, W. (C. 1849-51. V.-P. 1863-4.)

1853 Evans, Conway, M.D., 5, Tavistock-street, Covent Garden, W.C. (C. 1867-8.)

1875 Evans, Julian, A.M., M.D., 123, Finborough-road, Redcliffe-square, West Brompton, S.W.

1879 Eve, Frederic S., 125, Harley-street, W. (C. 1885-7.)

1876 Ewart, James Cossar, M.B., C.M., School of Medicine, Edinburgh.

1881 Ewart, Joseph, M.D., Montpellier Terrace, Brighton.

Elected

1877 EWART, WILLIAM, M.D., 33, Curzon-street, W. (C. 1889-1.)
‡1859 EWENS, JOHN, 14, Whiteladies-road, Clifton, Bristol.
1887 EYLES, CHARLES HENRY, Gold Coast Colony.

1889 FAIRBANK, FREDERICK ROYSTON, M.D., 59, Warrior-square, St. Leonard's-on-Sea.
1872 FAYRER, Sir JOSEPH, K.C.S.I., M.D. LL.D., F.R.S., 53, Wimpole-street, W. (C. 1880-2. V.-P. 1890-1.)
1872 FENN, EDWARD L., M.B., Grey Friars, Colchester.
1883 FENWICK, E. HURRY, 5, Old Burlington-street, W.
1872 FENWICK, JOHN C. J., M.D., 25, North-road, Durham.
1863 FENWICK, SAMUEL, M.D., 29, Harley-street, W.
1885 FÉRÉ, CHARLES, M.D., Médecin de Bicêtre; Boulevard St. Michel, 37, Paris.
1876 FINLAY, DAVID W., M.D., Aberdeen. (C. 1886-8.)
1859 FISHER, ALEXANDER, M.D., 2, Bruntsfield Gardens, Edinburgh.
1882 FLEMING, GEORGE, C.B., LL.D., 98, Tyrwhitt-road, St. John's, S.E.
1872 FORBES, DANIEL MACKAY, Shoreditch Infirmary, 204, Hoxton-street, N.
‡1866 FOSTER, Sir BALTHAZAR WALTER, M.D., M.P., 11, George-street, Hanover-square, W.
1872 FOTHERBY, HENRY J., M.D., Woodthorpe Cotes, Reigate.
1891 FOULERTON, ALEXANDER GRANT RUSSELL, 122, Brompton-road, S.W.
1880 FOWLER, JAMES KINGSTON, M.A., M.D., 35, Clarges-street, W. (C. 1887-8.)
1878 FOX, THOMAS COLCOTT, M.B., B.A., 14, Harley-street, W. (C. 1892.)
1858 FRANCIS, CHARLES RICHARD, M.B., Bengal Medical Establishment, Indian Army.
1886 FREEMAN, HENRY WILLIAM, 24, Circus, Bath.
O.M. FRERE, J. C.
1891 FRIPP, ALFRED DOWNING, M.B., B.S., 65, Harley-street, W.
1864 FRODSHAM, JOHN MILL, M.D., Streatham, S.W.

1880 GABBETT, HENRY SINGER, M.B., 20, Burlington-place, Eastbourne.
‡1858 GAIRDNER, WILLIAM TENNANT, M.D., LL.D.Edin., 225, St. Vincent-street, Glasgow. (V.-P. 1891-2.)
1890 GALLOWAY, JAMES, M.A., M.B., 16, Finsbury-circus, E.C.
1870 GALTON, JOHN H., M.D, 39, Anerley-road, Upper Norwood, S.E.
1855 GAMGEE, J.
L1846 GARROD, Sir ALFRED BARING, M.D., F.R.S., 10, Harley-street, W. (C. 1851. V.-P. 1863-5.)
1892 GARROD, ARCHIBALD EDWARD, M.D., 9, Chandos-street, W.
1879 GARSTANG, THOMAS WALTER HARROPP, Headingley House, Knutsford, Cheshire.
1872 GARTON, WILLIAM, M.D., Inglewood, Aughton, near Ormskirk, Lancashire.

Elected

1891 GASTER, AUGHEL, M.D., 34, Warwick-road, Maida-hill, W.

1880 GIBBES, HENRAGE, M.B., University of Michigan, Ann Arbor, Michigan, U.S.A.

L1853 GIBBON, SEPTIMUS, M.D., 39, Oxford-terrace, Hyde-park, W.

1878 GIBBONS, R. A., M.D., 29, Cadogan-place, S.W.

1876 GILL, JOHN, M.D., 31, Apsley-road, Clifton, Bristol.

1881 GLYNN, THOMAS ROBINSON, M.D., 62, Rodney-street, Liverpool.

1873 GODLEE, RICKMAN JOHN, M.B., M.S., 19, Wimpole-street, W. (C. 1877-80. 1891-2. S. 1887-9.)

1879 GODWIN, CHARLES HENRY YOUNG, Surgeon Major, Army; Victoria Hospital, Netley.

1878 GOLDING-BIRD, CUTHBERT H., M.B., 12, Queen Anne-street, W. (C. 1885-7.)

1890 GOODALL, E. WILBERFORCE, M.D., The Eastern Hospital, Homerton, N.E.

1871 GOODHART, JAMES FREDERIC, M.D., 25, Weymouth-street, W. (C. 1876-8, 1886-8. S. 1883-5. V.-P. 1892.)

1875 GOULD, ALFRED PEARCE, M.S., 16, Queen Anne-street, W. (C. 1883-5.)

1870 GOWERS, WILLIAM RICHARD, M.D., F.R.S., 50, Queen Anne-street, W. (C. 1878-9.)

L1858 GOWLLAND, PETER Y., 82, Gloucester-terrace, Hyde-park, W.

1888 GRANT, J. DUNDAS, M.A., M.D., C.M., 8, Upper Wimpole-street, W.

1867 GREEN, T. HENRY, M.D., 74, Wimpole-street, W. (C. 1871-3, 1878-9. S. 1875-6. V.-P. 1886-8.)

1873 GREENFIELD, WILLIAM SMITH, M.D., B.S., 7, Heriot-row, Edinburgh. (C. 1877-80.)

‡1855 GREENHILL, WILLIAM ALEXANDER, M.D., 5, The Croft, Hastings.

1886 GREVES, EDWIN HYLA, M.D., Rodney House, Suffolk-road, Bournemouth.

1885 GRIFFITH, WALTER SPENCER ANDERSON, M.B., 114, Harley-street, W.

1892 GRIFFITH, WILLIAM STOKES, M.B., B.C., 4, Bramham-gardens, S.W.

1887 GRIFFITHS, JOSEPH, M.B., C.M., 16, Panton-street, Cambridge.

1876 GRIFFITHS, THOMAS D., M.D., Hearne Lodge, Swansea.

1882 GROSS, CHARLES, M.D., M.S., 112, Westbourne-grove, W.

1880 GUNN, R. MARCUS, M.B., C.M., 54, Queen Anne-street, W.

1876 GWYTHER, JAMES, M.B.

1887 HABERSHON, SAMUEL HERBERT, M.D., 70, Brook-street, W.

L1851 HACON, E. DENNIS, 269, Mare-street, Hackney, N.E. (C. 1872.)

1879 HADDEN, WALTER BAUGH, M.D., 21, Welbeck-street, W. (C. 1886-8.)

1892 HADLEY, WILFRED JAMES, M.D., 16, Wimpole-street, W.

1882 HAIG, A., M.B., 7, Brook-street, W.

1877 HALLOWES, FREDERICK BLACKWOOD, Redhill, Surrey.

1890 HAMER, WILLIAM HEATON, M.B., Ladywell, Dartmouth Park Hill, Highgate, N.

Elected

1886 HAMILTON, DAVID JAMES, M.B., 1, Albyn-place, Aberdeen.
1890 HANDFIELD-JONES, MONTAGU, M.D., 35, Cavendish-square, W.
1886 HANDFORD, HENRY, M.D., 14, Regent-street, Nottingham.
1891 HANKIN, E. H., St. John's College, Cambridge.
1882 HARBINSON, ALEXANDER, M.D., County Lunatic Asylum, Lancaster.
L1848 HARE, CHARLES JOHN, M.D., Berkeley House, 15, Manchester-square, W. (C. 1852-4. V.-P.1874-7.)
L1856 HARLEY, GEORGE, M.D., F.R.S., 25, Harley-street, W. (C. 1862-5. V.-P. 1878-80.)
1872 HARRIS, HENRY, M.D., Trengweath-place, Redruth, Cornwall.
1879 HARRIS, VINCENT DORMER, M.D., 31, Wimpole-street, W.
L1858 HART, ERNEST, 38, Wimpole-street, W. (C. 1867-8.)
1891 HASLAN, WILLIAM F., 33, Paradise-street, Birmingham.
1870 HAWARD, JOHN WARRINGTON, 16, Savile-row, W. (C. 1879-81. V.-P. 1890-1.)
1886 HAWKINS, FRANCIS HENRY, M.B., 59, Wimpole-street, W.
1890 HAWKINS, HERBERT PENNELL, M.B., 38, Weymouth-street, W.
L1856 HEATH, CHRISTOPHER, 36, Cavendish-square, W. (C. 1866-7. V.-P. 1879-81.)
1881 HEBB, RICHARD G., M.D., 9, Suffolk-street, S.W. (C. 1891-2.)
1884 HEBBERT, CHARLES ALFRED.
1878 HELLIER, JOHN B., M.B., Headingley, Leeds.
1879 HENDERSON, GEORGE COURTENAY, M.D., Kingston, Jamaica, West Indies.
1869 HENSLEY, PHILIP J., M.D., 4, Henrietta-street, W.
1884 HERRINGHAM, WILMOT PARKER, M.B., 13, Upper Wimpole-street, W.
1855 HEWITT, GRAILY, M.D., 36, Berkeley-square, W. (C. 1865-7.)
1864 HICKMAN, WILLIAM, M.B., 5, Harley-street, W. (C. 1890-2.)
1875 HITCHCOCK, HARRY KNIGHT, M.D., Christowell, Branksome-park, Bournemouth, Hants.
1880 HOBSON, JOHN MORRISON, M.D., Glendalough, Morland-road, Croydon.
L1854 HOLMES, TIMOTHY, 18, Great Cumberland-place, W. (C. 1862-3. S. 1864-7. C. 1868. V.-P. 1869-71.)
L1850 HOLT, BARNARD WIGHT, 14, Savile-row, W. (C. 1853.)
O.M. HOLTHOUSE, CARSTEN. (C. 1852-4, V.-P. 1874-5.)
1878 HOOD, DONALD WILLIAM CHARLES, M.D., 43, Green-street, W.
1864 HOOD, WHARTON P., M.D., 11, Seymour-street, W.
1870 HOPE, WILLIAM, M.D., 54, Curzon-street, W.
1882 HOPKINS, JOHN, Central London Sick Asylum, Cleveland-street, W.
1879 HORROCKS, PETER, M.D., 26, St. Thomas's-street, S.E.
1883 HORSLEY, VICTOR, M.B., B.S., F.R.S., 25, Cavendish-square, W. (C. 1888-9.)
L1880 HOVELL, T. MARK, 105, Harley-street, W.
1875 HOWSE, HENRY GREENWAY, M.S., 59, Brook-street, W. (C. 1878-81.)
1884 HUDSON, CHARLES ELLIOTT LEOPOLD BARTON 6, Chandos-street, W.
L1856 HUDSON, JOHN, M.D., 11, Cork-street, W.

Elected

L1854 HULKE, JOHN WHITAKER, F.R.S., 10, Old Burlington-street, W. (C. 1863-5. S. 1868-72. V.-P. 1873-6, 1885-6. T. 1877-9. P. 1883-4.)

1874 HUMPHREYS, HENRY, M.D., Victoria-road, Fleet, Hants.

1883 HUMPHRY, Sir GEORGE MURRAY, M.D., LL.D., F.R.S. (PRESIDENT), University of Cambridge. (P. 1891-2.)

1888 HUNTER, WILLIAM, M.D., 61, Wimpole-street, W.

1852 HUTCHINSON, JONATHAN, F.R.S., 15, Cavendish-square, W. (C. 1856-9. V.-P. 1872-3, 1881-3. P. 1879-80.)

1882 HUTCHINSON, JONATHAN, jun., 12, Old Cavendish-street, W. (C. 1889-91.)

1884 HUTTON, HENRY RICHMOND, M.B., 8A, St. John-street, Manchester.

1889 HYSLOP, THEOPHILUS BULKELEY, M.B., C.M., Bethlem Royal Hospital, S.E.

1880 INGRAM, ERNEST FORTESCUE, Newcastle, Natal, S. Africa.

1886 JACKSON, ARTHUR MOLYNEUX, M.D., Middlesex County Asylum, Tooting, S.W.

1865 JACKSON, J. HUGHLINGS, M.D., F.R.S., 3, Manchester-square, W. (C. 1872-3. V.-P. 1888-9.)

1886 JACKSON, PHILIP J., 216, Great Dover-street, S.E.

1887 JACOB, ERNEST HENRY, M.D., 12, Park-street, Leeds.

1875 JALLAND, WILLIAM HAMERTON, St. Leonard's House, Museum-street, York.

1888 JAMES, J. T., 30, Harley-street, W.

‡1853 JARDINE, JOHN LEE, Capel, near Dorking, Surrey.

1881 JENNINGS, WILLIAM OSCAR, M.D., 8, Rue Roy, Paris.

1879 JESSOP, CHARLES MOORE, 98, Sutherland-avenue, W.

1866 JESSOP, THOMAS RICHARD, 31, Park-square, Leeds.

1878 JOHNSON, ARTHUR JUKES, Yorkville, Ontario, Canada.

1876 JOHNSON, CHARLES HENRY, Winton House, Basingstoke, Hants.

LO.M. JOHNSON, Sir GEORGE, M.D., F.R.S., 11, Savile-row, W. (C. 1846-50. V.-P. 1863-4, 1884-6. T. 1880-3.)

1888 JOHNSON, RAYMOND, M.B., B.S., 20, Weymouth-street, Portland-place, W.

1881 JOHNSTON, JOSEPH, M.D., 24, St. John's Wood-park, N.W.

1854 JOHNSTONE, ATHOL A. W., St. Moritz House, 61, Dyke-road, Brighton.

L1853 JONES, SYDNEY, M.B., 16, George-street, Hanover-square, W. (C. 1864-6. V.-P. 1886-7.)

1888 JONES, TALFOURD, M.B., Eastbourne.

1862 JONES, THOMAS RIDGE, M.D., 4, Chesham-place, S.W. (C. 1882-4.)

1886 JULER, HENRY EDWARD, 23, Cavendish-square, W.

1890 KANTHACK, A. A., M.B., B.S., St. John's College, Cambridge.

1867 KELLY, CHARLES, M.D., Broadwater-road, Worthing, Sussex. (C. 1874.)

L1846 KENT, THOMAS J., 89, Piccadilly, W.

Elected

1879 KESTEVEN, WILLIAM HENRY, 372, Camden-road, N.
1859 KIALLMARK, HENRY WALTER, 5, Pembridge-gardens, W. (C. 1875-6.)
1882 KIDD, PERCY, M.D., 60, Brook-street, W. (C. 1889-91.)
1867 KING, EDWIN HOLBOROW, Netley Court, Southampton.
1871 KING, ROBERT, M.B., Boyfield House, Moulton, Spalding, Lincolnshire.
L1852 KINGDON, J. ABERNETHY, 2, Bank-buildings, E.C.
1888 KYNSEY, WILLIAM RAYMOND, C.M.G., Colombo, Ceylon.

1878 LANCEREAUX, ETIENNE, M.D., 44, Rue de la Bienfaisance, Paris.
1882 LANE, WILLIAM ARBUTHNOT, M.B., M.S., 8, St. Thomas's-street, S.E. (C. 1891-2.)
1865 LANGTON, JOHN, 62, Harley-street, W. (C. 1882-4.)
1886 LANKESTER, HERBERT, M.D., 1, Elm-park-gardens, S.W.
1869 LARCHER, O., M.D.Par., 97, Rue de Passy, Paris. [M. Kliensieck, Libraire, Rue de Lille, 11, Paris, per Messrs. Longmans.]
1884 LARDER, HERBERT, Whitechapel Infirmary, Bakers-row, E.
1873 LATHAM, PETER WALLWORK, M.D., 17, Trumpington-street, Cambridge.
1876 LAW, WILLIAM THOMAS, M.D., 9, Norfolk-crescent, W.
1883 LAWFORD, JOHN BOWRING, M.D., C.M., 55, Queen Anne-street, W.
1853 LAWRENCE, HENRY JOHN HUGHES, Picton House, Llandowror, St. Clears. (C. 1873-5.)
1892 LAWRENCE, TURNER WILLIAM PELHAM, M.B., 138, Maida-vale, W.
1887 LAWSON, BERNARD, Timaru, Canterbury, New Zealand.
1859 LAWSON, GEORGE, 12, Harley-street, W. (C. 1870-1. V.-P. 1884-5.)
1879 LAYCOCK, GEORGE LOCKWOOD, M.B., Melbourne, Victoria, Australia.
1891 LAZARUS-BARLOW, WALTER, M.B.Sydney, 16, Bryanston-street.
1875 LEDIARD, HENRY AMBROSE, M.D., 41, Lowther-street, Carlisle.
L1852 LEE, HENRY, 9, Savile-row, W. (C. 1860-2. V.-P. 1875-6.)
1879 LEECH, DANIEL JOHN, M.D., 96, Mosley-street, Manchester.
1877 LEES, DAVID B., M.D., 22, Weymouth-street, W. (C. 1890-2.)
1867 LEES, JOSEPH, M.D., 21, Brixton-road, S.W.
1877 LEESON, JOHN RUDD, M.D., C.M., 6, Clifden-road, Twickenham.
1868 LEGG, JOHN WICKHAM, M.D. (C. 1874-5.)
1892 LEITH, ROBERT FRASER CALDIE, M.B., C.M., B.Sc., 129, Warrender-park-road, Edinburgh.
1884 LEONARD, HENRY JAMES, M.B., 279, Camden-road, N.
1892 LEUDET, THEODORE-EMILE, 49, Boulevard Cauchoise, Rouen, France.
1861 LICHTENBERG, GEORGE, M.D., 47, Finsbury-square, E.C.
1889 LIGHT, EDWIN MELLOR, M.B., B.C., The Infirmary, Leeds.
1877 LISTER, Sir JOSEPH, Bart., D.C.L., LLD., F.R.S., 12, Park-crescent, W. (C. 1880-2. V.-P. 1887-8, 1891-2.)
1889 LITTLE, JOHN FLETCHER, M.B., 60, Welbeck-street, W.
L1862 LITTLE, LOUIS S., China.
1878 LITTLEJOHN, SALTER G., M.B., C.M., Central London District Schools, Hanwell.

Elected

1874 LIVEING, EDWARD, M.D., 52, Queen Anne-street, W.
L1863 LIVEING, ROBERT, M.D., 11, Manchester-square, W. (C. 1876.)
1882 LOCKWOOD, C. B., 19, Upper Berkeley-street, W.
1876 LONGHURST, ARTHUR EDWIN TEMPLE, M.D., 4, Eaton Square, S.W. (C. 1885-7.)
1881 LUBBOCK, MONTAGU, M.D., 19, Grosvenor-street, W.
1873 LUCAS, R. CLEMENT, M.B., M.S., 18, Finsbury-square, E.C. (C. 1883-5.)
1880 LUND, EDWARD, 22, St. John-street, Manchester.
1879 LUNN, JOHN REUBEN, St. Marylebone Infirmary; Rackham-street, Ladbroke-grove-road, W.
1887 LYON, THOMAS GLOVER, M.D., 8, Finsbury-circus, E.C.

1871 MACCARTHY, JEREMIAH, M.A., 15, Finsbury-square, E.C. (C. 1878-80.)
1873 MCCONNELL, J. F.
1871 MAC CORMAC, Sir WILLIAM, 13, Harley-street, W. (C. 1878-80.)
1882 MACKENZIE, FREDERIC MORELL, 29, Hans-place, S.W.
1870 MACKENZIE, GEORGE WELLAND, 13, William-street, S.W.
1885 MACKENZIE, HECTOR WILLIAM GAVIN, 77, Lambeth Palace-road, S.E.
1870 MACKENZIE, JOHN T., Bombay, India.
1878 MACKENZIE, STEPHEN, M.D., 18, Cavendish-square, W. (C. 1890.)
1879 MACLAGAN, THOMAS JOHN, M.D., 9, Cadogan-place, S.W.
1865 MACLAURIN, HENRY NORMAND, M.D., 187, Macquarie-street, Sydney, New South Wales.
1876 MACNAMARA, CHARLES, 13, Grosvenor-street, W.
1879 MACREADY, JONATHAN FORSTER, 51, Queen Anne-street, W.
1885 MAGUIRE, ROBERT, M.D., 4, Seymour-street, W.
1877 MAKINS, GEORGE HENRY, 2, Queen-street, May Fair, W. (C. 1889-91.)
1887 MALCOLM, JOHN DAVID, M.B., C.M., 13, Portman-street, W.
1892 MANN, HAROLD EDWARD, Eastern Hospital, Homerton.
1890 MANSON, PATRICK, M.D., C.M., 21, Queen Anne-street, W.
1876 MAPLES, REGINALD, Kingsclere, near Newbury.
1868 MARSH, F. HOWARD, 30, Bruton-street, W. (C. 1876-7.) (V.-P. 1889-90.)
1887 MARTIN, SIDNEY, M.D., B.S., 10, Mansfield-street, W.
1889 MASON, DAVID JAMES, M.D., Rosemont, Maidenhead.
1867 MASON, PHILIP BROOKES, Burton-on-Trent.
1884 MAUDSLEY, HENRY CARR, M.D., 11, Spring-street, Melbourne, Victoria.
L1852 MAY, GEORGE, jun., M.B., Reading.
1888 MAY, WILLIAM PAGE, M.D., B.Sc., Goldburn, Eltham-road, Blackheath, S.E.
1881 MAYLARD, ALFRED ERNEST, M.B., 4, Berkeley-terrace, Glasgow.
1874 MEREDITH, WILLIAM APPLETON, M.B., 21, Manchester-square, W.
1859 MESSER, JOHN COCKBURN, M.D., Assistant Surgeon R.N.
1866 MICKLEY, GEORGE, M.A., M.B., St. Luke's Hospital, Old-street, E.C.
1882 MONEY, ANGEL, M.D.

Elected

1879 MOORE, NORMAN, M.D., 94, Gloucester-place, Portman-square, W. (C. 1885-7.)

1881 MOORE, THOMAS, 6, Lee-terrace, Blackheath, S.E.

1875 MORGAN, JOHN H., 68, Grosvenor-street, W. (C. 1886-8.)

1874 MORISON, ALEXANDER, M.D., C.M., Dunnottar, 115, Green-lanes, N.

1880 MORISON, BASIL GORDON, M.B., C.M., 70, Marquess-road, N.

1869 MORRIS, HENRY, M.A., M.B., 8, Cavendish-square, W. (C. 1877-9, 1884-6. S. 1881-3. V.-P. 1888-9.)

1879 MORRIS, MALCOLM ALEXANDER, 8, Harley-street, W.

1891 MORTON, CHARLES A., 24, St. Paul's-road, N.W.

1875 MORTON, JOHN, M.B., Guildford.

1884 MOTT, FREDERICK WALKER, M.D., 84, Wimpole-street, W. (C. 1891-2.)

1879 MOULLIN, CHARLES W. MANSELL, M.D., 69, Wimpole-street, W.

1878 MUMFORD, WILLIAM LUGAR, M.D., 12, Suffolk-street, Pall Mall, S.W.

1876 MUNRO, WILLIAM, M.D., C.M., Clarkefield, Fountain-street, Cheetham Hill, Manchester.

1885 MURRAY, HUBERT MONTAGUE, M.D., 27, Savile-row, W.

1864 MYERS, ARTHUR B. R., 43, Gloucester-street, Warwick-square, S.W. (C. 1872-3.)

1882 MYERS, A. T., M.D., 2, Manchester-square, W.

1887 MYERS, W. H., Fort Wayne, Indiana, U.S.A.

1887 NASON, EDWARD NOEL, M.B., 80, Abbey-street, Nuneaton.

1873 NETTLESHIP, EDWARD, 5, Wimpole-street, W. (C. 1882-4.)

1875 NEWBY, CHARLES HENRY, 15, Landport-terrace, Southsea, Hants.

1865 NEWMAN, WILLIAM, M.D., Stamford, Lincolnshire.

1868 NICHOLLS, JAMES, M.D., Trenarren, Newquay, Cornwall.

1876 NICHOLSON, JOHN FRANCIS, M.D., 29, Albion-street, Hull.

1878 NOOTT, WILLIAM MATHIAS, 8, Kensington-park-road, W.

L1864 NORTON, ARTHUR T., 101, Harley-street, W. (C. 1877-9.)

1883 NORVILL, FREDERIC HARVEY, M.B., Summerland, Yeovil, Somersetshire.

1856 NUNN, THOMAS WILLIAM, 8, Stratford-place, W. (C. 1864-6. V.-P. 1878-80.)

1871 NUNNELEY, Rev. FREDERICK BARHAM, M.D.

1880 O'CONNOR, BERNARD, M.D., Greenhill-park, Harlesden, N.W.

1873 O'FARRELL, GEORGE PLUNKETT, M.B., 19, Fitzwilliam-square, Dublin.

1880 OGILVIE, GEORGE, M.B., 22, Welbeck-street, W.

1880 OGILVIE, LESLIE, M.B., 46, Welbeck-street, W.

1850 OGLE, JOHN W., M.D., 30, Cavendish-square, W. (C. 1855-6. S. 1857-60. C. 1861-3. V.-P. 1865-8.)

1876 OLIVER, JOHN FERENS, M.D., 12, Old Elvet, Durham.

1888 OPENSHAW, THOMAS HORROCKS, M.B., B.S., 16, Wimpole-street, W.

1860 ORANGE, WILLIAM, M.D., 35, Cromwell-road, Brighton.

1875 ORD, WILLIAM MILLER, M.D., 37, Upper Brook-street, W. (C. 1880-2.)

Elected

1892 Ord, William Wallis, M.B., B.A., 32, Harley-street, W.
1879 Ormerod, J. A., M.D., 25, Upper Wimpole-street, W. (C. 1887-9.)
1881 Owen, Isambard, M.D., 40, Curzon-street, W.
1865 Owles, James Allden, M.D., Hill View, Woking, Surrey.

1875 Page, Herbert William, M.A., M.C. Cantab., 146, Harley-street, W. (C. 1889-91.)
1870 Paget, Sir James, Bart., D.C.L., LL.D., F.R.S., 1, Harewood-place, W. (P. 1887-8.)
1884 Paget, Stephen, 57, Wimpole-street, W.
1872 Parker, Robert William, 13, Welbeck-street, W. (C. 1881-3.)
1874 Parker, Rushton, M.B., B.S., 59, Rodney-street, Liverpool.
L1853 Parkinson, George, 50, Brook-street, W.
1882 Pasteur, William, M.D., 4, Chandos-street, W.
1885 Paul, Frank Thomas, 44, Rodney-street, Liverpool.
1865 Pavy, Frederick William, M.D., F.R.S., 35, Grosvenor-street, W. (C. 1872-4. V.-P. 1891-2.)
1868 Payne, Joseph Frank, M.D., 78, Wimpole-street, W. (C. 1873-5, 1883-5. S. 1880-2. V.-P. 1888-9.)
1872 Pearce, Joseph Chaning, M.D., C.M., Montague House, St. Lawrence-on-Sea, Kent.
1863 Pearson, David R., M.D., 23, Upper Phillimore-place, W.
1884 Pedley, F. Newland, 32, Devonshire-place, Portland-place, W.
1879 Peel, Robert, 130, Collins-street East, Melbourne, Victoria.
1889 Penberthy, John, Royal Veterinary College, Camden Town, N.W.
1887 Penrose, Francis George, M.D., 4, Harley-street, W.
1884 Pepper, Augustus Joseph, M.B., C.M., 13, Wimpole-street, W.
1888 Perry, Edwin Cooper, M.B., The College, Guy's Hospital, S.E.
1878 Philipps, Sutherland Rees, M.D., St. Ann's-heath, Virginia Water, Chertsey.
1871 Phillips, Charles Douglas F., M.D., 10, Henrietta-street, W.
1878 Phillips, John Walter, 30, Stanley-street, West Melbourne, Victoria.
1863 Pick, Thomas Pickering, 18, Portman-street, W. (C. 1870-1. V.-P. 1885-7.)
1867 Pitt, Edward G., M.D.
1884 Pitt, George Newton, M.D., 24, St. Thomas's-street, S.E. (C. 1890-2.)
1876 Pitts, Bernard, M.A., M.B., 31, Harley-street, W. (C. 1888-90.)
1887 Pitts, Robert Zaccheus, Springfield, Chelmsford.
1886 Pocock, Walter, 374, Brixton-road, S.W.
1883 Poland, John, 4, St. Thomas's-street, Southwark, S.E.
1882 Pollard, Bilton, 24, Harley-street, W.
L1846 Pollock, George D. (Trustee), 36, Grosvenor-street, W. (S. 1850-3. C. 1854-6. V.-P. 1863-5. P. 1875-6.)
1850 Pollock, James Edward, M.D., 52, Upper Brook-street, W. (C. 1862-4. V.-P. 1879-81.)

Elected

1870 POORE, GEORGE VIVIAN, M.D., 30, Wimpole-street, W. (C. 1883-5.)
1876 PORT, HEINRICH, M.D., 48, Finsbury-square, E.C.
L1879 POTTER, HENRY PERCY, St. Mary Abbotts' Infirmary, Marloes-road, Kensington, W.
1866 POWELL, RICHARD DOUGLAS, M.D., 62, Wimpole-street, W. (C. 1873-5, 1881-3. S. 1877-9. V.-P. 1887-8.)
1884 POWER, D'ARCY, M.A., M.B., 26, Bloomsbury-square, W.C. (C. 1891-2.)
1865 POWER, HENRY, 37A, Great Cumberland-place, W. (C. 1876-7.)
1887 PRATT, WILLIAM SUTTON, Weedon, Northamptonshire.
1884 PRICE, J. A. P., M.D., 41, Castle-street, Reading.
1888 PRIESTLEY, R. C., M.B., 81, Linden-gardens, W.
L1856 PRIESTLEY, WILLIAM OVEREND, M.D., 17, Hertford-street, W.
1888 PRIMROSE, ALEXANDER, M.B., C.M. 196, Simcoe-street, Toronto, Canada.
1882 PRINGLE, J. J., M.B., 23, Lower Seymour-street, W.
L1848 PURNELL, JOHN JAMES, Woodlands, Streatham-hill, S.W. (C. 1858-61.)
1865 PYE-SMITH, PHILIP HENRY, M.D., F.R.S., 48, Brook-street, W. (C. 1874-7. V.-P. 1890-1.)

LO.M. QUAIN, Sir RICHARD, Bart., M.D., LL.D., F.R.S. (TRUSTEE), 67, Harley-street, W. (C. 1846-51. S. 1852-6. T. 1857-68. *Pres.* 1869-70. V.-P. 1871-3.)

1884 RAKE, BEAVEN NEAVE, M.D., Leper Asylum, Trinidad.
1872 RALFE, CHARLES HENRY, M.D., M.A., 26, Queen Anne-street, W. (C. 1877-9.)
1857 RANKE, HENRY, M.D., Munich.
‡1890 RANSOM, WILLIAM BRAMWELL, M.D., The Pavement, Nottingham.
1865 RASCH, ADOLPHUS A., M.D., 7, South-street, Finsbury-square, E.C.
1891 RATCLIFFE, JOSEPH RILEY, M.B., The General Hospital, Birmingham.
1887 RAVEN, THOMAS FRANCIS, Broadstairs, Kent.
1870 RAY, EDWARD REYNOLDS, Dulwich Village, S.E.
1875 REID, ROBERT WILLIAM, M.D., C.M., 8, Queen's-gardens, Aberdeen.
1881 RENNER, WILLIAM, M.R.C.S., Wilberforce-street, Free Town, Sierra Leone.
1854 REYNOLDS, J. RUSSELL, M.D., F.R.S., 88, Grosvenor-street, W. (C. 1868-9.)
1871 RICHARDS, J. PEEKE, 6, Freeland-road, Ealing, W.
1866 RIVINGTON, WALTER, M.S., 95, Wimpole-street, W.
‡1865 ROBERTS, DAVID LLOYD, M.D., 11, St. John's-street, Manchester.
1871 ROBERTS, FREDERICK THOMAS, M.D., 102, Harley-street, W. (C. 1883-5.)
1878 ROBERTS, WILLIAM HOWLAND, M.D., Surgeon, Madras Army.
1888 ROBERTSON, ROBERT, M.D., The Bungalow, Ventnor, Isle of Wight.
1885 ROBINSON, ARTHUR HENRY, M.D., Mile End Infirmary, Bancroft-road, N.E.
1887 ROBINSON, HENRY BETHAM, M.B., 59, Lambeth Palace-road, S.E.
1882 ROBINSON, TOM, M.D., 9, Princes-street, Cavendish-Square, W.

Elected

1888 Rolleston, H. D., M.B., B.C., 13, Upper Wimpole-street, W.

L1858 Rose, Henry Cooper, M.D., Penrose House, Hampstead, N.W. (C. 1873-4.)

1876 Rose, William, M.B., B.S., 17, Harley-st., W.

1879 Ross, James, M.D., C.M., 335, Oxford-street, Manchester.

1875 Rossiter, George Frederick, Cairo Lodge, Weston-super-Mare.

1877 Roth, Bernard, 29, Queen Anne-street.

1888 Roughton, Edmund Wilkinson, 33, Westbourne-terrace, W.

1891 Rouillard, Laurent Antoine John, M.B., St. Thomas's Hospital, S.E.

1858 Rouse, James, 2, Wilton-street, S.W.

1887 Roy, Charles Smart, F.R.S., M.D., M.A., &c., University of Cambridge.

1891 Ruffer, Marc Armand, M.D., 19, Iddesleigh Mansions, Westminster, S.W.

1891 Russell, William, M.D., 46, Albany-street, Edinburgh.

1869 Rutherford, William, M.D., F.R.S., 14, Douglas-crescent, Edinburgh.

1882 Sainsbury, Harrington, M.D., 63, Welbeck-street, W.

1853 Salter, S. James A., M.B., F.R.S., Basingfield, near Basingstoke, Hants. (C. 1861-3. V.-P. 1880-2.)

1854 Sanderson, John Burdon, M.D., D.C.L.Durham, F.R.S., 50, Banbury-road, Oxford. (C. 1864-7. V.-P. 1873-4.)

1875 Sangster, Charles, 148, Lambeth-road, S.E.

1877 Sankey, H. R. O., M.B., Boreatton Park, Baschurch, Salop.

1886 Saundby, Robert, M.D., 83a, Edmund-street, Birmingham.

1871 Saunders, Charles Edward, M.D., Sussex County Lunatic Asylum, Hayward's Heath.

1890 Saunders, Frederick William, M.B., B.C., 17, Barkston-gardens, South Kensington, S.W.

1873 Savage, George Henry, M.D., 3, Henrietta-street, Cavendish-square, W. (C. 1881-3.)

1882 Savill, Thomas Dixon, M.D., Paddington Infirmary, 285, Harrow-road, W.

1891 Schoerstein, Gustave Isidore, M.B., B.S., London Hospital Medical College, E.

1877 Semon, Felix, M.D., 39, Wimpole-street, W. (C. 1885-7.)

1872 Sergeant, Edward, Town Hall, Bolton, Lancashire.

1876 Sharkey, Seymour J., M.D., 2, Portland-place, W. (C. 1884-6.)

1880 Shattock, Samuel G. (Hon. Secretary), 4, Crescent-road, The Downs, Wimbledon. (C. 1885-7. S. 1890-2.)

1885 Shaw, Lauriston Elgie, M.D., 10, St. Thomas's-street, S.E.

1884 Sheild, Arthur Marmaduke, M.B., B.S., 20, Stratford-place, Oxford-street, W.

1886 Sherrington, Charles Scott, M.B., 27, St. George's-square, S.W.

L1856 Shillitoe, Buxton, 2, Frederick's-place, E.C.

L1855 Sibley, Septimus W., The Hermitage, Bletchingley, Surrey. (C. 1863-5. V.-P. 1879-81.)

Elected

1887 SIBLEY, WALTER KNOWELEY, 7, Harley-street, W.
1875 SIDDALL, JOSEPH BOWER, M.D., C.M., Conybeare, Northam, Bideford.
1880 SILCOCK, A. QUARRY, M.D., B.S., 52, Harley-street, W. (C. 1888-90.)
1892 SILK, JOHN FREDERICK WILLIAM, M.D., 29, Weymouth-street, W.
1866 SIMS, FRANCIS MANLEY BOLDERO, 12, Hertford-street, W.
1892 SLATER, CHARLES, M.B., 16, Northwick-terrace, N.W.
1887 SMALLPEICE, WILLIAM DONALD, 42, Queen Anne's-gate, S.W.
‡1875 SMEE, ALFRED HUTCHINSON, The Grange, Hackbridge, Carshalton, Surrey.
1879 SMITH, E. NOBLE, 24, Queen Anne-street, W.
1887 SMITH, FREDERICK JOHN, M.B., 4, Christopher-street, Finsbury-square, E.C.
1875 SMITH, GEORGE JOHN MALCOLM, M.B., Hurstpierpoint, Sussex.
1872 SMITH, GILBART, M.D., 68, Harley-street, W.
1878 SMITH, HERBERT URMSON, M.B., Cape Colony.
1873 SMITH, RICHARD T., M.D., 53, Haverstock-hill, N.W.
1883 SMITH, ROBERT PERCY, M.D., Bethlem Royal Hospital, St. George's Road, S.E.
1869 SMITH, ROBERT SHINGLETON, M.D., Deepholm, Clifton Park, Bristol.
1856 SMITH, THOMAS, 5, Stratford-place, W. (C. 1867-9. V.-P. 1877-8.)
1866 SMITH, WILLIAM, Melbourne, Australia.
1870 SMITH, WILLIAM JOHNSON, Seamen's Hospital, Greenwich, S.E. (C. 1879-81.)
L1869 SMITH, WILLIAM WILBERFORCE, M.D., 14, Stratford-place, W.
1870 SNOW, WILLIAM VICARY, M.D., Richmond Gardens, Bournemouth.
1888 SOLLY, ERNEST, M.B., Royal Free Hospital, Gray's Inn-road, W.C.
1868 SOUTHEY, REGINALD, M.D., 32, Grosvenor-road, Pimlico. (C. 1882-4.)
1887 SPENCER, WALTER GEORGE, M.B., 35, Brook-street, W.
1888 SPICER, ROBERT HENRY SCANES, M.D., 28, Welbeck-street, W.
1861 SQUIRE, ALEXANDER BALMANNO, M.B., 24, Weymouth-street, W.
1885 SQUIRE, JOHN EDWARD, M.D., 53, Harley-street, W.
1890 STABB, EWEN CARTHEW, St. Thomas's Hospital, Albert-embankment, S.E.
1889 STEWART, EDWARD, M.D.
L1854 STEWART, WILLIAM EDWARD, 16, Harley-street, W.
1891 STILES, HAROLD JALLAND, M.B., C.M., 5, Castle-terrace, Edinburgh.
1879 STIRLING, EDWARD CHARLES, Adelaide, South Australia [care of Messrs. Elder & Co., 7, St. Helen's Place, E.C.].
1883 STOKER, GEORGE, 14, Hertford-street, W.
1881 STOKES, HENRY FRASER, 2, Highbury-crescent, N.
1884 STONHAM, CHARLES, 4, Harley-street, W.
1875 STURGE, W. A., M.D., 29, Boulevard Dubouchage, Nice.
L1871 SUTHERLAND, HENRY, M.D., 6, Richmond-terrace, Whitehall, S.W.
1882 SUTTON, JOHN BLAND, 48, Queen Anne-street, W. (C. 1887-90.)
‡1867 SWAIN, WILLIAM PAUL, 17, The Crescent, Plymouth.

Elected

1881 SYMONDS, CHARTERS JAMES, M.S., 26, Weymouth-street, Portland-place, W. (C. 1886-8.)

1870 TAIT, ROBERT LAWSON, 7, The Crescent, Birmingham.
1886 TARGETT, JAMES HENRY, M.B., M.S., 6, St. Thomas's-street, S.E.
1891 TATE, WALTER WILLIAM HUNT, 2, The Terrace, Camden-square, N.W.
1864 TATHAM, JOHN, 12, George-street, Hanover-square, W.
1870 TAY, WARREN, 4, Finsbury-square, E.C. (C. 1881-2.)
1871 TAYLOR, FREDERICK, M.D., 20, Wimpole-street, W. (C. 1879-81.)
1885 TAYLOR, HENRY H., 10, Brunswick-place, Brighton.
1892 TAYLOR, JAMES, M.D.Edin., 45, Weymouth-street, W.
1880 TAYLOR, SEYMOUR, M.D., M.C., 16, Seymour-street, W.
1879 THIN, GEORGE, M.D., 22, Queen Anne-street, W. (C. 1889-90.)
1870 THOMAS, JOHN DAVIES, M.D., 52, North-terrace, Adelaide, South Australia [care of Mr. H. K. Lewis, Gower-street].
L1852 THOMPSON, Sir HENRY, Knt., 35, Wimpole-street, W. (S. 1859-63. C. 1865-7. V.-P. 1868-70.)
1891 THOMSON, HENRY ALEXIS, M.D., 2, Coates-crescent, Edinburgh.
1884 THOMSON, JOHN, M.B., C.M., 18, Walker-street, Edinburgh.
1874 THORNTON, JOHN KNOWSLEY, M.B., 22, Portman-street, W.
1872 THORNTON, WILLIAM PUGIN, 35, St. George's-road, Canterbury.
1880 TIRARD, NESTOR ISIDORE, M.D., 28, Weymouth-street, W.
1884 TIVY, WILLIAM JAMES, 8, Lansdowne-place, Clifton, Bristol.
1856 TOMES, Sir JOHN, F.R.S., Upwood Gorse, Caterham, Surrey. (C. 1867-9.
1882 TOOTH, H. H., M.D., 34, Harley-street, W. (C. 1892.)
1886 TOTSUKA, KANKAI.
L1872 TOWNSEND, THOMAS SUTTON, 68, Queen's Gate, S.W.
1888 TREVELYAN, E. F., M.D., Seamen's Hospital, Greenwich, S.E.
1881 TREVES, FREDERICK, 6, Wimpole-street, W. (C. 1887-90.)
1851 TROTTER, JOHN W., Bossall Vicarage, York. (C. 1865-9.)
1859 TRUMAN, EDWIN THOMAS, 23, Old Burlington-street, W.
1888 TUBBY, ALFRED HERBERT, M.B., 39, Finsbury-circus, E.C.
1867 TUCKWELL, HENRY MATTHEWS, M.D., 64, High-street, Oxford.
1858 TUDOR, JOHN, Dorchester, Dorset.
L1875 TURNER, FRANCIS CHARLEWOOD, M.D. (HON. SECRETARY), 15, Finsbury-square, E.C. (C. 1884-6. S. 1891-2.)
1882 TURNER, GEORGE ROBERTSON, 49, Green-street, W.
1863 TURNER, JAMES SMITH, 12, George-street, Hanover-square, W.
1890 TURNER, WILLIAM ALDREN, M.B., 13, Queen Anne-street, W.
1858 TURTLE, FREDERICK, Clifton Lodge, Woodford, Essex.
1880 TYSON, WILLIAM JOSEPH, M.D., 10, Langhorne-gardens, Folkestone.

1867 VENNING, EDGCOMBE, 30, Cadogan-place, S.W.
1889 VOELCKER, ARTHUR FRANCIS, M.D., B.S., 13, Welbeck-street, W.

L1867 WAGSTAFFE, WILLIAM WARWICK, B.A., Purleigh, St. John's-hill, Sevenoaks. (C. 1874, 1878-80. S. 1875-7.)

Elected

LO.M. WAITE, CHARLES D., M.D., 3, Old Burlington-street, W.

1885 WAKLEY, THOMAS, jun., 5, Queen's-gate, S.W.

1881 WALLER, BRYAN CHARLES, M.D., Masongill House, Cowan-bridge, Kirkby-Lonsdale.

1890 WALLIS, FREDERICK CHARLES, M.B., M.S., 18, St. James's-street, S.W.

1888 WALSHAM, HUGH, M.A., M.B., B.C., 32, New Cavendish-street, W.

1873 WALSHAM, WILLIAM JOHNSON, M.B., C.M., 27, Weymouth-street, W. (C. 1881-3.)

1859 WALTERS, JOHN, M.B., Reigate, Surrey.

1892 WARD, ALLAN OGIER, M.D.Edin., Lansdowne House, Tottenham.

1889 WASHBOURN, JOHN WYCHENFORD, M.D., Guy's Hospital, S.E.

1877 WATERHOUSE, CHARLES, M.B., M.C., Carl Ludwigstrasse, Währing, Vienna.

1891 WATERHOUSE, HERBERT FURNIVALL, M.D., C.M., 81, Wimpole-street, W.

1880 DE WATTEVILLE, ARMAND, M.A., M.B., 30, Welbeck-street, W.

1890 WEBB, CHARLES FRERE, M.D., New-street House, Basingstoke.

L1858 WEBER, HERMANN, M.D., 10, Grosvenor-street, W. (C. 1867-70. V.-P. 1878-80.)

1876 WEIR, ARCHIBALD, M.D., St. Mungho's, Great Malvern.

1864 WELCH, THOMAS DAVIES, M.D., Fairmount, Frith-hill, Godalming, Surrey.

1853 WELLS, Sir THOMAS SPENCER, Bart., 3, Upper Grosvenor-street, W. (C. 1865-8. V.-P. 1876-7.)

L1851 WEST, CHARLES, M.D., Kenilworth, Eaton-road, West Brighton. (C. 1856-7.)

1877 WEST, SAMUEL, M.D., 15, Wimpole-street, W. (C.1884-6, 1891-2. S. 1889-90.)

1888 WETHERED, FRANK J., M.D., 34, Queen Anne-street, W.

1891 WHEATON, SAMUEL WALTON, M.D., 52, The Chase, Clapham Common, S.W.

1867 WHIPHAM, THOMAS TILLYER, M.B., 11, Grosvenor-street, W. (C. 1880-2.)

1869 WHIPPLE, JOHN H. C., M.D., Army Medical Staff.

1877 WHITE, CHARLES HAYDON, 20, Shakespeare-street, Nottingham.

1891 WHITE, GILBERT B. MOWER, M.B., B.S., 105, Gower-street, W.C.

1881 WHITE, WILLIAM HALE, M.D., 65, Harley-street, W. (C. 1888-90.)

1886 WHITE, WILLIAM HENRY, M.D., 43, Weymouth-street, W.

‡1868 WHITEHEAD, WALTER, 24, St. Ann's-square, Manchester.

1877 WHITMORE, WILLIAM TICKLE, 7, Arlington-street, S.W.

1870 WICKSTEED, FRANCIS WILLIAM, Chester House, Weston-super-Mare.

1869 WILKIN, JOHN F., M.D., M.C., New Beckenham, Kent.

1871 WILKINSON, J. SEBASTIAN, New Zealand.

1855 WILKS, SAMUEL, M.D., F.R.S. (TRUSTEE), 72, Grosvenor-street, W. (C. 1857-60. V.-P. 1869-72, 1883-5. P. 1881-2.)

1879 WILLCOCKS, FREDERICK, M.D., 14, Mandeville-place, W.

Elected

1886 WILLETT, EDGAR WILLIAM, M.B., 25, Welbeck-street, W.

1869 WILLIAMS, ALBERT, M.D. (Travelling).

‡1858 WILLIAMS, CHARLES, 48, Prince of Wales-road, Norwich.

1866 WILLIAMS, CHARLES THEODORE, M.D., 2, Upper Brook-street, W. (C. 1875-8.)

1881 WILLIAMS, DAWSON, M.D., B.S., 25, Old Burlington-street, W.

1872 WILLIAMS, JOHN, M.D., 63, Brook-street, W. (C. 1878-80.)

1864 WILLIAMS, W. RHYS, M.D., Linden House, Bertie-road, Leamington.

1881 WILLIAMS, W. ROGER, 28, Winckley-square, Preston.

1876 WILLIAMSON, JAMES MANN, M.D., Ventnor, Isle of Wight.

1863 WILLIS, FRANCIS, M.D., The Spa, Braceborough, Stamford.

1889 WILSON, ALBERT, Leytonstone, Essex.

1888 WILSON, CLAUDE, M.D., C.M., 6, York-road, Tunbridge Wells.

1859 WILSON, EDWARD THOMAS, M.B., Montpelier-terrace, Cheltenham.

1859 WILSON, ROBERT JAMES, 7, Warrior-square, St. Leonards-on-Sea.

1891 WILSON, THEODORE STACEY, M.B., C.M., 65, Temple-row, Birmingham.

‡1861 WINDSOR, THOMAS, Medical Library, Boston, Mass., U.S. [care of B. F. Stevens, 4, Trafalgar-square, W.].

1889 WINGRAVE, V. HAROLD WYATT, 7, Taviton-street, Gordon-square, W.C.

1874 WISEMAN, JOHN GREAVES, Dearden-street, Ossett, Yorkshire.

1865 WITHERBY, WILLIAM H., M.D., Pitt-place, Coombe, Croydon.

1887 WOOD, T. OUTTERSON, M.D., 40, Margaret-street, W.

1876 WOOD, WILLIAM EDWARD RAMSDEN, M.A., M.D., The Priory, Roehampton, S.W.

1883 WOODCOCK, JOHN ROSTRON, 155, Hagley-road, Birmingham.

1883 WOODHEAD, GERMAN SIMS, M.D., Beverley, Nightingale-lane, Balham, S.W. (C. 1891-2.)

1879 WOODWARD, G. P. M., M.D., Deputy Surgeon-General; Sydney, New South Wales.

1884 WORTS, EDWIN, 6, Trinity Street, Colchester.

1869 WYMAN, WILLIAM S., M.D., Red Brae, 18, Putney-hill, S.W.

1890 WYNNE, EDWARD T., M.B., County Asylum, Rainhill, Prescot.

1884 WYNTER, WALTER ESSEX, 30, Upper Berkeley-street, W.

1872 YOUNG, HENRY, M.B., Monte Video, South America.

ANNUAL REPORT OF COUNCIL, 1891-92.

PRESENTED AT THE ANNUAL MEETING, MAY 17TH, 1892.

YOUR Council has to report but a small increase in the number of members, a result due to the lamentably large number of deaths. Twenty-five new members have been admitted, of whom nineteen are resident and six non-resident. There have been eight resignations and fifteen deaths; to these must be added the death of one honorary member, viz. Professor Bruecke. The list of deaths comprises, in addition to that of Professor Bruecke, Sir William Bowman, Mr. Beaney, Dr. J. H. Bennet, Dr. Alfred Carpenter, Sir Prescot Hewett, Bart., Mr. Berkeley Hill, Dr. Kershaw, Sir Morell Mackenzie, Dr. Robert Martin, Mr. Edward Milner, Mr. John Morgan, Dr. F. G. Reed, Dr. H. J. Sanderson, Dr. Semple, and Dr. Henry G. Sutton.

Three members have compounded on the terms of the sliding scale introduced not long since.

The debate held during the session on Phagocytosis and Immunity has been second to none in the interest which it has raised; each of the three meetings over which it extended was prolonged beyond the usual hour, and very fully attended both by members and visitors.

During the past three years the annual expenditure of the Society has exceeded its annual income. It has, indeed, been necessary to sell stock in order to meet expenses, and this has been done at the present time in order that a new financial year may correspond with the next session of the Society.

By the sale of stock to the value of £162 5*s.* 7*d.* the Society, after the payment of all bills, is now ready to start another year with a balance of £120 19*s.* 7*d.*, and with the sum of £1000 invested.

The chief explanation of deficiency in income is due to the very low scale of Composition Fees introduced a few years since. This scale was based upon that adopted by the Royal Medical and Chirurgical Society. The latter Society has recently found it necessary to raise the scale, which appears to have been calculated far too low. The Council asks the General Meeting convened on May 17th, 1892, to sanction the suspension of the Law [XIX] relating to Composition Fees, pending its reconstruction by a special committee appointed for the purpose.

The Council has, moreover, resolved to put some limitation to the number of microscopes allowed to each member on any single occasion, and in other ways to reduce expenditure; and it feels assured, after careful investigation, that by these different methods the financial position of the Society may be rendered quite secure.

Signed, on behalf of the Council,

G. M. Humphry, *President.*

May 3rd, 1892.

THE PATHOLOGICAL SOCIETY OF LONDON,

Cr. *In Account with the Treasurer*, WILLIAM CAYLEY, ESQ., M.D., *44th Session*, 1891–92. **Dr.**

From 1st May, 1891, *to 30th April*, 1892.

	£	s.	d.	£	s.	d.
By *Balance* in Treasurer's hands on 1st May, 1891				33	3	0
By *Subscriptions:*						
341 paid direct 11 „ through Bank 352	369	12	0			
22 Admissions at 21*s.*	23	2	0			
10 Non-Resident Compositions at £2 2*s.*	21	0	0			
3 Life (Resident) Compositions	19	19	0			
				433	13	0
By *Sale of Transactions:*						
By Publisher	69	9	3			
„ Assist. Sec.	13	14	0			
„ Composition	10	10	0			
				93	13	3
By *Dividends*				31	6	0
By *Sale of Consols* (£167 15*s.* 1*d.*), net sum realised				162	5	7
				£754	0	10

	£	s.	d.	£	s.	d.
To *Meetings:*						
Rent	105	0	0			
Refreshments	36	15	0			
R. Coldrey	7	10	0			
Microscopes	42	4	0			
				191	9	
Transactions:						
Printing, Binding, &c., of Vol. XLII.	231	5	0			
Illustrations	121	13	9			
				352	18	9
Secretariat and Treasury:						
Assistant Sec.	31	10	0			
Commission to Collector (including balance from last year)	22	14	0			
Petty Cash	13	7	0			
Bank Charges	2	17	0			
				70	8	
The Virchow Testimonial				18	5	6
				633	1	3
Balance in hand				120	19	7
				£754	0	10

Audited and found correct, May 9th, 1892,

W. BRUCE CLARKE, H. H. CLUTTON, } *Auditors.*

W. CAYLEY, M.D., *Treasurer.*
April 29th, 1892.

SAMUEL G. SHATTOCK, F. C. TURNER, M.D., } *Hon. Secs.*

Amount of Investments in hands of Trustees—Consols, £1000.

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REPORT.

SESSION 1891-1892.

I. DISEASES, ETC., OF THE NERVOUS SYSTEM.

1. *Subdural hæmorrhage.*

By E. T. Wynne, M.B.

I have brought these specimens and drawings before the Society, not because I have any new facts to communicate; but as subdural hæmorrhage (not the result of injury) is rarely seen in hospital *post-mortem* rooms, and as the series seems to illustrate very well the mode of formation of so-called pachymeningitis hæmorrhagica, I hope they will be of interest to members.

The opinion is gaining ground that this condition is, at least in the insane, not of inflammatory origin; that is to say, is not the result of an inflammation of the dura mater. As to whether chronic inflammation of the pia is a necessary condition for its production I will not now discuss, but I think that congestive storms such as are so common in general paralysis (the class of patients in which the condition is most frequent) are not of themselves sufficient to cause it.

Let me first describe a typical specimen of pachymeningitis hæmorrhagica, such as specimens 5 and 6. On removing the dura mater a thick layer of clotted blood comes away with it. The central portion may have the appearance of a false membrane, stained a rusty or dirty brown colour; but towards the periphery, if not of very old standing, there is simply clotted blood, fading at the margin into an extremely thin, faintly yellow film. This

film may be lifted up with forceps and stripped off with perfect ease, showing the dura mater quite normal, as depicted in Drawing A. As the centre is approached the clot is found to be tied down here and there, more or less firmly to the dura, by minute vessels. If these portions are forcibly stripped, nothing abnormal beyond the presence of these vessels is seen. The clot is here becoming organised. The new vessels arising from this organisation often rupture, producing a secondary hæmorrhage into the false membrane. Specimen 7 shows a small hæmorrhage thus formed in a hæmatoma of old standing, and under the microscope is a similar hæmorrhage in a more recent case.

In large hæmatomata one constantly notices a very distinct lamination, like that in aneurysms. This, I think, is caused partly by the movements of the brain, partly by recurrent hæmorrhages, and partly by the gradual admixture of the blood with subdural fluid.

I have here given a brief description of the facts, without considering the condition from either a hæmorrhagic or inflammatory point of view. An excellent description from the inflammatory point of view is given by Rindfleish. He, agreeing with Virchow, regards the initial lesion as an exudation from an inflamed dura mater, which rapidly becomes organised. The new-formed structure pours out a fresh exudation, which also becomes organised. Hæmorrhages occur always somewhere between the youngest exudation and the dura—that is, never on the arachnoid side of the formation. They may form pools the size of a man's hand, and push the newly formed exudation away from the rest of the formation. He says that in these cases the youngest exudation can always be seen as a cobweb-like film stretching over the hæmatoma. This film, he states, was formerly erroneously thought to be a "peripheral, capsular coagulum of fibrin." Here, I think, is Rindfleish's error. He mistakes this "peripheral, capsular coagulum of fibrin" for an exudation from the already organised effusion. This peripheral film which stretches all over the blood-clot *is* a coagulum of fibrin, and its real nature is clearly shown in my specimens. Its presence is easily recognised in specimens 5 and 6. The microscopic section 2 leaves no doubt to my mind of its nature. I will, for convenience, refer to the rough drawing I have made of this section.

Layer 1 is almost structureless, but under a high power is clearly

seen to be composed of red cells partly broken down and fibrin threads. Layer 2 is rich in small round nuclei, among which delicate vessels are beginning to make their way from layer 3, which is undergoing organisation. Now layers 1 and 2 constitute the film mentioned above, and layer 1 is a capsular coagulum of fibrin, containing red cells. These two layers are nothing more than a clot in a condition analogous to the "buffy coat" of physiologists. That is, the red and white cells have become separated into more or less distinct layers.

Rindfleish seems to me to have started with the assumption that a specimen like No. 7 is an earlier condition than such as 5 or 6.

I will now briefly describe the specimens exhibited to-night. Nos. 1 and 2 and drawing A show the earliest traces of this condition. They show mere specks of blood, sticking, but not fixed to the dura mater. The dura is quite healthy. No. 3 shows a similar condition, but the blood is spattered over the dura like lymph in an early case of pericarditis. The dura shows no trace of inflammation. Nos. 4, 5, and 6 are well-developed specimens, such as I have described above. B and C are drawings of the fresh state. In No. 7, of which D is a drawing, is presented a late stage in the history of these formations. Here the blood of the original hæmorrhage has been entirely absorbed, nothing but a delicate almost white membrane is left. In the drawing it is much too pink. It has split into two layers, between which a clot has formed from the rupture of the delicate vessels which run in the membrane. This last is an example of so-called arachnoid cyst.

Under the microscope I have placed sections from this last specimen and from No. 5, as samples of sections cut from a number of my own cases and from specimens belonging to Dr. Wigglesworth. The first shows the entire disappearance of the hæmorrhage and its replacement by vascular membrane.

The second section shows an organising hæmatoma, with a secondary hæmorrhage and the limiting layer of fibrin and red cells. In neither section does the dura mater show signs of inflammation.

I think the above facts demonstrate fairly clearly the hæmorrhagic origin of pachymeningitis hæmorrhagica. As to the origin of the blood I can say but little. Several writers have localised it in the pia mater. Dr. Wigglesworth has published a case in

which he was able to ascertain the exact vessel in pia from which the blood had come. Drawing C shows a vessel from which the hæmorrhage may have come. Besides the pia and dura there is a third source from which blood may come; namely, small vessels which pass from the dura to pia, especially in the fronto-parietal region, which is one of the commonest places for the hæmatoma to appear. If the pia is always the source of the hæmorrhage it is strange that subarachnoid hæmorrhage in any large amount should be so rare, while large effusions of serum are common, and, on the other hand, large hæmatomata in the subdural space not infrequent and large effusions of serum (at least in my experience) very uncommon.

In concluding, I wish to express my indebtedness to Dr. Wigglesworth, the Medical Superintendent of Rainhill Asylum, for his kind permission to show the drawings, which were made for him from specimens which I obtained from the Asylum *post-mortem* rooms.

December 15*th*, 1891.

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2. *Double subdural cysts of hæmorrhagic origin.*

By G. Newton Pitt, M.D.

The specimen consists of a portion of the dura mater of the left side, to which is loosely attached a thin ochreous membrane ¼ mm., thick, which forms part of the wall of a cyst which lay in the arachnoid space. The cyst contained about six or seven ounces of serous fluid and recent blood-clot; it extended from the longitudinal sinus for about three inches downwards. The anterior and posterior portions of the cyst have been removed, but the remainder measures 4 × 3 × ¾ inch. The outer layer can be easily peeled off the dura mater, and the inner was not adherent to the pia arachnoid. A similar but smaller cyst containing three to four ounces of fluid occupied the left side. The cysts occupied especially the frontal regions.

The cyst wall is smooth and polished on its interior surface; the ochreous pigment was chiefly on the outer and rougher surface.

On the inner surface of the parietal portion of the wall was a

thin layer of blood clot which has now been washed away. The brain, which otherwise appeared normal, was markedly compressed.

Microscopically.—The dura mater, measuring ·7 mm. in thickness, is quite normal, except that there are a few cells in some elongated spaces close to the adventitious membrane, but there is no evidence that the dura mater is inflamed.

The false membrane, ·3 mm. thick, is formed of embryonic connective tissue containing numerous cells, some round, others becoming fibroblasts. It is vascular, and the laminæ of fibrous tissue are arranged parallel to the surface; no endothelial layer can be detected.

Clinical history.—J. J—, æt. 46, for a year or two had suffered with severe frontal headaches. When first seen by Mr. G. H. Knapp, to whom I am indebted for the specimen and the history, no paralysis or other abnormal physical signs were noticed. His wife stated, however, that he had twitching on the right side, especially at night-time.

Two weeks before his death it was noticed that he had twitchings confined to his arm and face, and that he rolled his eyes upwards and chiefly to the right. When he grasped an object tightly with either hand his arm gave a decided jerk after a few seconds. He is also said to have had some twitching of his legs. From this time he became dull and apathetic; no paralysis was demonstrable, and he was able to walk across the room.

A week before his death he suddenly became drowsy, and did not recognise his relations; he also had dysphagia. He gradually became more comatose until his death; until the coma was profound he had no incontinence. There was no anæsthesia. The temperature and pulse were normal throughout. The urine was free from albumen. The optic discs were not examined.

The cases of subdural cysts which have been observed since Mr. Prescott Hewitt's paper in the 'Med.-Chir. Transactions' of 1845, corroborate his view that this condition is the result of a hæmorrhage into the subdural space, which laminates on the interior of the dura mater, and forms a cyst-wall of embryonic connective tissue around itself. In the present, which is a typical case, the inner surface of the membrane is smooth and firm, its tissue is ochreous in colour, its contents serum, with more or less altered blood-clot. The cyst-wall was not at all attached to the pia arachnoid, and only loosely to dura mater.

There is no evidence of any inflammation of the dura mater, nor of any bands across the sac, such as would probably have formed had it owned inflammatory origin.

The cyst is undoubtedly due to hæmorrhages into the subdural space on either side, but the history is not complete enough to enable us to determine its source. The blood in cases of general paralysis of the insane comes from the cerebral veins, which the wasted brain fails to support. Blows upon the head producing subdural hæmorrhage may produce these cysts on one or both sides of the brain, as Drs. Hewett, Greenfield, Ogle, and othes have proved. Chronic alcoholism, typhus and relapsing fevers have been shown by Kremiansky and others to have been the cause in many cases.

No cases have been shown at this Society since 1878, if we except a recent subdural hæmorrhage published by Dr. Turner in vol. xxxvi, p. 16, and it is most exceptional to meet with cases outside the mortuaries of lunatic asylums. *November 3rd*, 1891.

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3. *Fibroma of dura mater indenting the cortex, without symptoms.*

By Edgar Willett.

The specimen shown, consisted of the right half of a brain and cerebellum, together with a portion of the dura mater of the same side. Attached to the latter by a broad base there was a globular tumour, measuring nearly two inches in diameter; this had caused a large depression in the cortex. The dura mater was adherent, but not very firmly so, to the parietal bone, on the inner surface of which was a broad flat exostosis, with one or two slightly projecting prominences. The base of this exostosis was deeply grooved by nutrient vessels. This piece of bone was also shown; its internal surface was quite smooth, and displayed no evidence of the irregularity seen on the inner table.

The portion of cortical substance implicated was that situated over the upper third of the fissure of Rolando, consequently directly over important centres in the motor area. The pia mater and

arachnoid, though considerably thinned, were continued over the depression, and were not adherent to the tumour, except at one spot.

The interest in the case lies in the fact that no symptoms whatever existed during life; the patient was a healthy woman, aged 38. There was no history of syphilis, nor had she ever suffered from fits. She had never given any signs of insanity, had never had any form of paralysis, and had not complained of headache. She was quite well until four days before her death, which occurred from acute double pneumonia. She remained conscious until six hours before her death.

Microscopical examination of the tumour (specimens of which were shown) proved it to be a fibroma, and the explanation of the absence of symptoms during life is no doubt to be found in the fact that the growth of the tumour was exceedingly slow.

The specimen is now in the Museum of St. Bartholomew's Hospital, Series xxx, No. 2465A. *May 3rd*, 1892.

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4. *Cyst containing fatty matters between the frontal lobes of the brain.* (*Card specimen.*)

By H. D. Rolleston, M.D.

There is a smooth-walled cyst, as large as an orange, situated between the two frontal lobes on their inferior aspect. The two frontal lobes are equally indented by the cyst, which appeared to grow between the layers of the falx cerebri. The walls of the cyst show only fibrous tissue under the microscope. The cyst contains solid opaque white matter exactly like lard. Microscopically nothing but amorphous fat, no cells or hairs.

At the *post-mortem* there was clear solid matter on the surfaces of both the frontal lobes around the cyst, composed of crystalline fat, probably derived from the cysts. The anterior fossa of the skull behind the crista galli was very deeply depressed by the cyst. The apex of the right frontal lobe was firmly adherent to dura mater. Around the cyst there were numerous small fibrous tumours, which microscopically were composed of well-formed fibrous tissue, enclosing a little fatty matter like that in the cyst.

These bodies were probably pachionian bodies hypertrophied from the irritation of the large cyst.

The cyst was completely enclosed by the dura mater.

What the origin of this cyst was, is not plain. The fact of its containing fat suggests the idea that it is a dermoid. But its position, outside the dura mater, between the layers of the falx cerebri and between the inferior surfaces of the frontal lobes, the constitution of its wall, viz. fibrous tissue, without any epidermal lining, and the absence of any cellular forms in its contents, do not support such a view.

From a woman, aged 47 years, who died in St. George's Hospital from the effects of burns. She had for years suffered from epileptic fits, which had of late become more frequent, occurring every day.

At one time she had been in an asylum for two years.

March 15th, 1892.

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5. *Sections from the Rolandic region of the brain from five cases of death with chorea, showing lesions of some of the large pyramidal cells of the cortex.*

By F. Charlewood Turner, M.D.

[With Plate I, fig. 1.]

The cases from which the sections of brain cortex now exhibited were obtained were the following:

Case 1.—*Pregnancy; severe chorea; abortion; septicæmia.*—Emily B—, aged 19, married, pregnant three months, was admitted into the London Hospital on January 19th, 1876, and died March 2nd. Choreic movements commenced three weeks before admission, and were very violent. She had never had rheumatism. A systolic bruit was heard at the apex of heart, and a trace of albumen was found in the urine. Abortion was induced, and was followed by fatal puerperal septicæmia.

Post-mortem.—Uterus ulcerated; pyæmia; pneumonia; pleurisy; infarcts in spleen; heart fatty and contracted.

CASE 2.—*Acute nephritis; endocarditis; severe chorea; hæmaturia; intestinal hæmorrhage.*—Emily S—, aged 17, admitted October 28th, 1881, and died December 15th. Symptoms of acute nephritis for a week before admission. Systolic bruit appeared, and choreic movements came on in hospital, albuminuria and dropsy continuing. The choreic movements, became very violent, with insomnia, but were less severe after beginning of December. Then hæmaturia and hæmorrhage from intestine. No history of rheumatism.

Post-mortem.—Kidneys enlarged with swelled cortex and slightly granular surface, and not peeling easily. Mitral valve thickened and bordered with small gelatinous vegetations capped with recent clot. Recent pleurisy and pneumonia at right apex. Bronchioles filled with airless pus. Slight peritonitis; patches of congestion in large and small intestine; mesenteric glands enlarged and congested; brain apparently normal.

CASE 3.—*Morbus cordis; albuminuria; acute chorea.*—Esther R—, aged 12, was admitted February 26th, 1886, and died June 7th. There was a history of severe rheumatic fever, and of œdema of legs and face three months. The heart was enlarged, and a double mitral and a systolic aortic murmur were heard. The urine was scanty, but contained no albumen on admission. This subsequently appeared and increased gradually to three quarters, with failing heart. On May 28th slight choreiform movements were observed. They became severe a week before death, ceasing during the last two days.

Post-mortem.—The heart was distended; the mitral valve stenosed, with granulations along its edges. The lungs were compressed by fluid; there were a few nodules of consolidation in the left, and lymph on right lung. Liver, spleen, and kidneys congested and firm. Lower limbs and forearms were œdematous; body wasted. The skin over the elbows was rough. Brain of normal appearance.

CASE 4.—*Endocarditis; acute chorea.*—Beatrice M. G—, aged 16, admitted December 14th, 1881, and died December 17th. Subacute rheumatism two months before admission. Choreic move-

ments first observed on December 10th, chiefly on the left side. The movements increased in severity, with screaming. She was admitted with severe bilateral chorea; noisy and screaming at night. She answered questions fairly, but seemed to have delusions. The heart's action was very rapid; no murmur heard throughout. She became comatose on December 17th, and died the same day.

The autopsy showed endocarditis with lines of granulations along the borders of both mitral and aortic curtains.

CASE 5.—*Acute chorea; recent endocarditis.*—Blanche J—, aged 16, was admitted December 28th, 1891, and died January 5th, 1892. Choreic movements had been observed four weeks before admission, and were attributed to a fright from a runaway horse one week previously. There was a history of another fright three months before admission. The movements became very violent, and she was anæsthetised several times, and injections of hyoscyamin were given. A deep-seated abscess appeared in the neck and was opened. Her temperature rose to 101° towards the end. A systolic mitral bruit was heard.

The autopsy showed recent endocarditis of the form commonly associated with severe and fatal chorea.

The sections now exhibited, which were taken from the Rolandic region of the brain of each of these cases, and which are arranged in the same order, all show conspicuous changes in many of the larger pyramidal cells in the deeper layers of the cortex.

In the first three specimens, from Cases 1, 2, and 3, several greatly enlarged nerve-cells, of rounded outline and swollen appearance, are conspicuous in this part of the cortex under a low power ($\frac{3}{4}''$) as shown. They are most conspicuous in the first specimen, less so in the third. -This drawing, made for me by Mr. Hollick (see Plate I, fig. 1), shows the appearance presented by two of the more affected pyramidal cells, shown in the first specimen, when seen under a higher power ($\frac{1}{6}''$). The left hand figure shows a very large and swelled pyramidal cell and some apparently normal nerve-cells adjacent to it. In the altered cell the outline, though not lost, is filled out and rounded at the angles; the protoplasm is cloudy and dense-looking, and more fully stained than in the normal cells, and defined at the bases of the processes, indicating a great swelling up of the body of the cell. The nucleus is ob-

DESCRIPTION OF PLATE I.

Fig. 1 illustrating Dr. Charlewood Turner's paper on Chorea. (Page 8.)

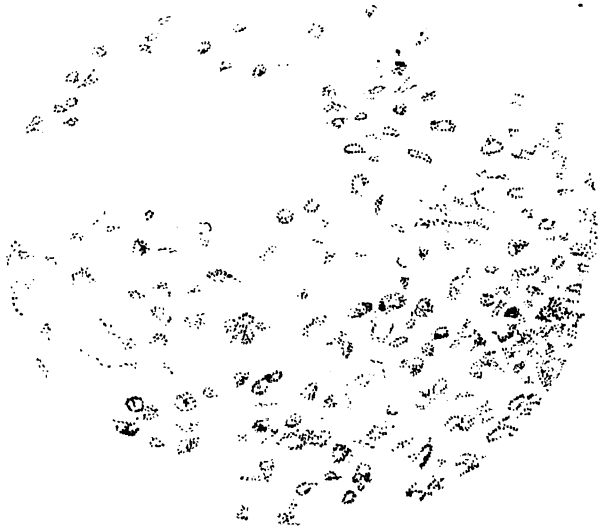
From drawings by A. T. Hollick.

FIG. 1.—(*a*) Part of a section from the Rolandic region of the brain, from a fatal case of chorea in a girl aged 19 years, showing a swelled and deformed pyramidal cell in the deeper layers of the cortex, with contiguous pyramidal cells apparently normal. In the swollen cell the protoplasm and the nucleus are granular, and more fully stained than in the other nerve-cells. (× 300.)

(*b*) A greatly swollen pyramidal cell in the same region of the cortex from another part of the same section. The natural outline of the cell is lost, and the nucleus is quite obscured in the granular and hazy protoplasm of the cell body. (× 300.)

Fig. 2 illustrating Dr. Sibley's paper on Inoculated Tuberculosis of Snakes. (Page 189.)

Lung stained with eosine and then by Gram's method, showing tubercle bacilli in rings in the leucocytes; the outlines and nuclei of the leucocytes are not shown. (Zeiss D. oc. 2.)



scured by the mass of cloudy protoplasm, but still visible from its fuller colour. The right hand figure shows a still more changed pyramidal cell, in which the normal outline is almost lost, and in which no nucleus is visible; a condition of great œdematous swelling by serous imbibition, presumably recoverable unless in its highest grade.

Sections 2 and 3 show similar lesions of the large pyramidal cells in similar positions, though not quite to the same extent. Sections 4 and 5, which are exhibited under a higher power ($\frac{1}{8}''$), show similar lesions of the same region of the cortex. The affected nerve-cells in these last specimens, though discernible, are not conspicuous under the lower power, as in the first three specimens.

The greater degree of the lesions observable in the former cases is, I think, attributable to the fact that in each of these cases the chorea, with which the patient ultimately died, was superinduced upon, or complicated with other lesions profoundly affecting the systemic nutrition—in Case 1 with puerperal septicæmia, in Cases 2 and 3 with albuminuria and endocarditis—a combination of adverse nutritive conditions tending to aggravate the effects of the nutritive disturbances of the brain with which the choreic symptoms were associated, and thus to present them in a magnified form.

Sections from the anterior and posterior extremities of the hemispheres in Cases 1, 2, 4, and 5 show similar lesions which are distinguishable under the lower power ($\frac{1}{4}''$). But in none of the sections from these parts in Cases 1 and 2 were there any cells so conspicuously affected as those in the Rolandic region. The difference in the lesions of the pyramidal cells found in the Rolandic and other regions is less notable in Cases 4 and 5.

In all the sections examined similar lesions of less, or of slight, degree are observable in many pyramidal cells under the higher power.

As regards the pathological significance of these cortical lesions in relation to chorea, I would submit—

1. That the clinical phenomena of ordinary cases of chorea are indicative of a structural lesion of the brain, and are not attributable to a nutritive derangement, with functional inhibition only, of the central nervous system, as in the case of hysterical paraplegia, where the volition is in abeyance, but can *at once* be excited by a sufficient and properly directed stimulus, or as in the case of an epileptic subject, in whom a fit occurs in apparent health under

certain predisposing and exciting influences. In such cases a defective nervous system reacts abnormally, under certain conditions, to stimuli of an ordinary kind. But in the clinical course of an ordinary case of acute chorea, the successive stages of ingravescence, of more or less uniform and prolonged persistence, and of subsidence often rapid and, it may be, quite "spontaneous," are more in correspondence with the course of inflammatory and febrile disorders, and of syphilitic and other structural lesions of the brain.

2. That the lesions shown are in accordance both with the clinical phenomena of chorea and with the conditions associated with their occurrence, with which, on the other hand, those vascular lesions, to which the occurrence of chorea has been attributed, do not accord either in their pathogeny and pathogenic potentiality, so far as is known, or in their observed anatomical features.

The loss of volitional control over the movements of the limbs without motor paralysis, and the intellectual dulness, which are the distinctive clinical phenomena of chorea, indicate a lesion, or functional inhibition, of the *cortex* of the brain. There is an increased reflex and emotional reaction, from want of control by the higher centres, and, it may be, from an increased sensitiveness of the spinal centres and central ganglia.

The clinical course of (typical) chorea further indicates a recoverable lesion of the nerve-tissues for the most part, though the indefinite persistence in severe cases of some loss of volitional control is indicative of destruction of some of the nerve-cells, to be made up for by the subsequent development and education of others in their place.

A mere œdematous swelling of the nerve-cells of the cortex of the brain, such as is seen in my specimens, is wholly in accordance with these observed clinical facts.

And such lesions, indicative of a too severe and too prolonged nutritive defect in these structures, are in accordance also with the pathogenic conditions with which the occurrence of chorea is associated, which all tend to prejudicially affect the nutrition of the higher cerebral structures.

The age and sex of those most liable to chorea involve a notable degree of "*instability*" of the higher and actively developing convolutional nervous tissues, *i. e.* an especial liability in them to suffer a relatively great disturbance of the blood supply to these

tissues from sensory or emotional excitement, even of moderate degree, such as constitutes the obvious, or presumptive, determining factor in the causation of chorea.

And the condition of debility from anæmia, rheumatism, or other cause, which constitutes the second condition predisposing to chorea, must increase this instability, and further heighten the injurious effect on the cortical tissues of any sensory or emotional excitement, and increase the frequency of such disturbances so produced; thus contributing with the constitutional state to the occurrence and subsequent aggravation of lesions of the pyramidal cells of the cortex, such as my specimens exhibit.

As regards the vascular lesions, to which some have attributed the phenomena of chorea, I think that the *embolic* hypothesis may be excluded, because the etiological conditions predisposing to chorea—sex, temperament, anæmia, &c.—have no relation to embolism, the pathogenic conditions of which, on the other hand —ulcerative endocarditis or endarteritis—have no relation to the occurrence of chorea. But it may be said that, setting this aside, any conditions tending to cause structural lesions of the nerve-cells must tend also to cause structural lesions of the small vessels supplying them, and thus to lead to thrombosis. But (1) the vascular system is little liable to structural lesions, independently of lesions of the surrounding tissues, in the youthful subjects of chorea, excepting (α) in conditions of systemic infection, as in specific infectious disease of severe type, in *ulcerative* endocarditis of destructive kind, in syphilis or tuberculosis, or (β) where the general nutrition is profoundly affected, as in scorbutic conditions; and (2) where such vascular lesions have been found in the central nervous system in cases of fatal chorea, their observed occurrence chiefly in the central ganglia and cord, is opposed to the supposition that there was any connection between them and the symptoms of chorea. It seems much more likely that these thromboses were due to extreme depression, or "typhoid state," of the patients when moribund.

It is certain, at all events, that structural lesions of the extravascular, and highly specialised, pyramidal nerve-cells would result from a nutritive disturbance insufficient to affect the vessels, directly in contact with the blood flowing through them, and possessing a higher vital resistance in correspondence with their far lower specialisation.

That this was so in the cases from which my specimens were taken, is evidenced by the absence of any appearance of vascular thrombosis in connection with the lesions of the pyramidal cells.

3. As regards the question, whether the occurrence of a lesion of the pyramidal cells of the cerebral cortex, seen to be so conspicuously changed in my specimens, was really the cause of the symptoms of chorea, or whether those lesions may not have been *wholly due* to the exhaustion of the patients in a moribund state, I think there is no doubt that they were in part due to that cause in every instance, and in great part also, in my first three specimens, to the concurrent existence of systemic nutritive disturbance complicating the pathological state. Such lesions of nerve-cells, being evidence of nutritive defect of the cerebral tissue of a certain degree and duration, would be looked for in all conditions thus severely affecting the cerebral functions; and I have sections from cases of fatal acute plumbism with cerebral symptoms, of uræmia, and others, in which such lesions occur, distinguishable under a low power of the microscope ($\frac{1}{5}''$). But in none of these sections have I found any lesion of the nerve-cells approaching those shown in the first three sections. I am thus led to the conclusion that these more striking nerve-cell lesions were in part due to the nutritive disturbance of the brain which caused the chorea in these patients.

And I infer from the evidence of nerve-cell lesions in these and the other sections, that, in accordance with the inference deducible from the clinical facts, the phenomena of chorea are due to structural lesions of the pyramidal cells of the cerebral cortex of the kind, though not of the degree, seen in these sections from severe and fatal cases—lesions of a kind producible by disturbance of the nutrition of the brain from various causes, and giving rise to the phenomena of chorea, when resulting from disturbances of the central nervous system which have determined an attack of that disorder, by the particular manner in which they are distributed in the cerebral cortex under such circumstances.

May 17th, 1892.

6. *Cyst of the left hemisphere of the brain, causing marked atrophy of the convolutions of that side, and of the left hemisphere generally.* (*Card specimen.*)

By JAMES GALLOWAY, M.B.

THE specimen shows an elongated cavity stretching in the white substance of the left cerebral hemisphere, from the frontal into the parietal region of the brain. At its posterior extremity the cavity turns upwards, and comes almost to the surface behind the ascending parietal convolution. The cavity is about one inch in diameter, and when quite fresh was seen to be lined by a distinct delicate membrane. The cavity contained no blood clot, nor any obvious traces of blood pigment. It was quite independent of the lateral ventricle. The convolutions of the frontal and parietal lobes are seen to be markedly atrophied, and the whole hemisphere is much smaller than the other.

The patient from whom the specimen was obtained, was admitted into the Bethnal Green House Lunatic Asylum in March, 1887, "in a state of mental depression with delusions of conspiracy." The attack was due to alcoholism, and he had suffered severely from syphilis.

In May, 1887, he had a complete and sudden attack of right hemiplegia, without convulsions, and unattended with unconsciousness. He subsequently developed post-hemiplegic rigidity and contraction of the right side.

In June, 1889, he had a convulsive seizure of short duration, which was not well observed by his attendant.

The patient died on 10th November, 1891, from the effects of morbus cordis of long duration, remaining melancholic, and having delusions to the end.

The cyst described seems, therefore, to have resulted from hæmorrhage, but is peculiar on account of its extent, and from the fact that it was probably followed by the marked atrophy of the left cerebral hemisphere which is so obvious.

I am indebted to Dr. J. K. Will, the Medical Superintendent, for the specimen. *November 17th*, 1891.

7. *A case of tumour of the spinal meninges.*

By J. Jackson Clarke, M.B.

Edith C—, aged 38, was admitted into St. Mary's Hospital, under Dr. Broadbent, on October 22nd, 1888, complaining of pain in the back and abdomen. She remembered straining her back when lifting something, and getting wet through and her clothes drying upon her as she was walking home. A month after this exposure and twelve months before admission, when trying to run, she noticed a pain in the back, which has been present more or less ever since. It was wont to come on toward evening, and compelled her to seek medical advice. She was sent into the country where after, as she thinks, catching cold, the pain became so much worse that she had to be held down when it came on. It often caused her to vomit, and she had attacks of shivering. She was treated by injections of morphia. One of these administered over the seat of the pain caused an abscess which was incised, and for two days after this the patient was free from pain.

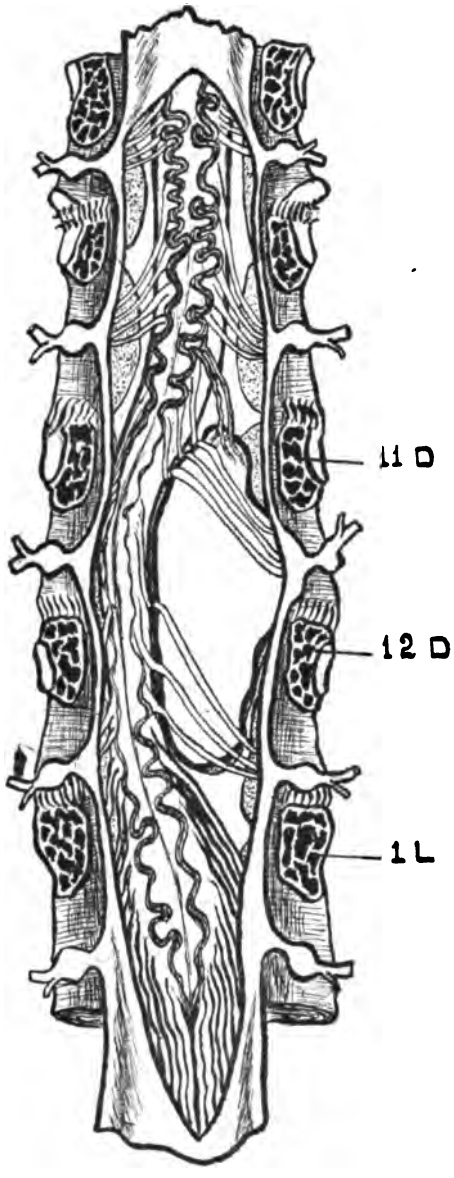
On admission the patient is described as a well-nourished middle-aged woman, of a dusky complexion.

Examination of the nervous system for cerebral symptoms gave negative results.

Examination of the spine showed absence of deformity. There was no tenderness at the seat of the pain, either when the vertebræ were pressed upon directly or when pressure was applied to the head. The patient complained of an aching, gnawing pain, commencing about two inches to the right of the spinous processes of the third and fourth lumbar vertebræ, and running outwards along the lower border of the last rib, and forwards just above the anterior superior iliac spine, and gradually extending across the abdomen as it increased in severity. At the same time this pain was felt round the right half of the body, there was pain beginning at the point where the right great sciatic nerve leaves the pelvis, and extending to the knee.

Sensation.—Over the lower part of the abdomen sensation to touch was slightly impaired, two points being felt as one at a distance of a quarter of an inch.

FIG. 1.



Part of the spinal cord with the tumour and its nutrient vessels, are represented with the bodies of the last four dorsal and of the first lumbar vertebræ. The posterior roots of the eleventh and twelfth dorsal nerves cross the back of the tumour. The arachnoid has been omitted. The tumour lay within it. All the parts are drawn the natural size. (From a drawing by the author.)

Reflexes.—Ankle-clonus was present on the right side, both knee-jerks were exaggerated.

Course of the case.—The patient vomited frequently during the attacks of the pain.

On October 31st it was noted that the plantar reflex of the right side was diminished.

On November 2nd the patient said that the pain began on the front of the abdomen and travelled to the right to the spine, reversing the usual direction.

6th.—The left plantar reflex was diminished.

12th.—The plantar reflexes were obtained only now and then. During an attack of pain, both plantar reflexes were absent, both knee-jerks were exaggerated, and there was ankle-clonus on both sides, most marked on the right. After ankle-clonus had been produced, there was twitching of the calf-muscles on the right side lasting one minute.

19th.—A good plantar reflex on both sides at the first attempt, but on trying again there was no reaction.

December 13th.—Patellar reflex more marked on left than on right side. Plantar reflexes very slight, more marked on left side.

19th.—Sensation delayed over one second in the right leg below the knee and about half a second on the left side.

January 3rd.—Patient complains of shooting pains in both legs. Plantar reflex present on both sides.

4th.—On the dorsum of the left foot heat interpreted as pain.

14th (Dr. Broadbent).—Sensations much impaired, especially on the outer side of the right leg. Plantar reflex exaggerated on the right side. Ankle-clonus present on both sides.

14th.—Dr. Broadbent having already diagnosed a growth of the spinal cord called a consultation of the other physicians and the surgeons of St. Mary's Hospital. All concurred in the diagnosis, and the patient was advised most strongly to undergo operation. After conferring with her friends, the patient decided not to follow this advice and left the hospital to die, three years later, of exhaustion due to most extensive bedsores.

The sketch (see fig. 1) shows the tumour and its chief relations. The account I have given in the Catalogue of the Museum of St. Mary's Hospital is as follows:

"(No. 768.) Lower part of a spinal column opened from behind showing a tumour on the right side of the cord which it

compresses. The upper end of the tumour is opposite the upper part of the eleventh dorsal vertebra, and it extends to the lower border of the twelfth. The posterior roots of the eleventh and twelfth dorsal nerves are stretched over the tumour and were slightly adherent to it. The tumour is encapsuled. Its vascular supply consists of a branch of the right posterior spinal artery with a companion vein. It was adherent to the edge of the ligamentum denticulatum and to the dura mater, but the adhesions were easily broken down with the finger. The arachnoid was adherent to the outside of the tumour. The microscope showed the growth to be a myxo-fibroma."

I may add that the operation could have been easily performed, and the case might have made a companion to that published by Dr. Gowers and Mr. V. Horsley in the 'Transactions' of the Royal Medical and Chirurgical Society for 1888.

It is to be regretted that the patient obstinately refused to profit by Dr. Broadbent's brilliant and absolutely accurate diagnosis. I should here like to thank Messrs. Bown and Handfield-Jones, in whose care the patient was at the time of her death, and who with great difficulty secured the parts of the spinal column and cord for the Museum of St. Mary's Hospital. *November 3rd*, 1891.

II. DISEASES, ETC., OF THE ORGANS OF CIRCULATION.

1. *Chronic tubercular pericarditis with effusion.*

By H. D. Rolleston, M.D.

The specimen shows the pericardium and heart from a child aged 9 months, who was admitted in a moribund condition into St. George's Hospital.

At the *post-mortem* there was tubercular meningitis, tubercular ulcers on the ileum; caseous mesenteric glands and caseous tubercle in the spleen.

Caseous tubercle was scattered through both lungs; the bronchial glands were caseous and enlarged and were adherent to the pericardium.

The pericardial sac was greatly enlarged, and almost hid the lungs from view when the sternum was removed; externally it was red and rough; when opened about 3 oz. of clear yellowish fluid ran out. The parietal layer of the pericardium was everywhere greatly thickened, and was so rigid that it did not collapse. Anteriorly there was a raised, thick, prominent area, which appeared red, as if from extravasation of blood into its substance.

The internal surface of the parietal layer of the pericardium was covered by a layer of easily detached reticulated lymph.

The heart was covered by the thickened opaque visceral layer of the pericardium, and lay at the back of the pericardium tethered by the great vessels.

There were no intra-pericardial adhesions, the cavity of the pericardium being distended, and the parietal and visceral layers kept apart by the chronic effusion.

Microscopically, the thickened parietal layer of the pericardium showed newly-formed fibrous tissue containing numerous small blood-vessels and giant-cell systems.

Dr. C. Slater, who also kindly examined the specimens, reported that "the tubercles in the pericardium showed tubercle bacilli, which were mainly in the giant cells, but also occurred between the small cells."

This is a case of chronic tubercular pericarditis with effusion. Three cases of tubercular pericarditis are described by Dr. Bristowe in 'Pathological Transactions'[1] in patients aged 21, 20, 13 years, and by Sir D. Duckworth[2] in a baby only eight months old, but the association of a chronically thickened pericardial sac, free from adhesions to the heart, and a clear effusion is not recorded.

November 3rd, 1891.

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2. *Acute pericarditis set up by perforation of the aorta, the patient living six days.* (*Card specimen.*)

By W. Lee Dickinson.

From a coach-builder, aged 34, who died in St. George's Hospital, August 19th, 1891.

The specimen shows acute pericarditis, stenosis of the mitral valve, extreme stenosis of the aortic valve, the segments of which are calcified, and a perforation of the aorta above the left cusp (possibly in connection with a minute aneurysm).

The chief interest of the specimen consists in that the pericarditis was set up by the perforation, as shown by the excess of lymph at this point; and that the man survived the onset of this pericarditis at least six days.

In the recent state the pericardium was distended by a litre of highly sanious serum. *May 17th*, 1892.

[1] Vol. xii, p. 63.
[2] Vol. xxvi, p. 246.

3. *Ulcerative endocarditis, with hæmorrhage on the left, and softening of the right side of the brain.*

By F. Charlewood Turner, M.D.

The specimens shown are the heart and brain of a brewer's labourer, aged 45, who was admitted into the London Hospital on September 18th, 1891, a short time after an attack of left hemiplegia, which came on suddenly with pain in the head and vertigo, but without loss of consciousness. There was partial recovery until a sudden and fatal apoplectic attack, of which he died on October 29th, forty-one days after the hemiplegic attack.

The brain shows a large and firm black clot in the substance of the *left* hemisphere, which had separated the corpus striatum from the white matter external and anterior to it, ploughing up the latter nearly up to the grey matter of the convolutions, and projected into the lateral ventricle. There was no extravasation of blood on the surface of the brain.

In the *right* hemisphere there is an extensive tract of softening in the white substance of the temporo-sphenoidal lobe and contiguous parts, external, anterior, and posterior to the corpus striatum, and involving the corpus striatum itself. In the horizontal section of the brain it extends forwards as far as the genu of the corpus callosum, and posteriorly it involves the anterior wall of the descending cornu of the ventricle. The softened tissue was uncoloured with blood.

At the base of the brain, the right middle cerebral artery, with the extremity of the internal carotid on the same side, is completely plugged by a decolorised thrombus. This was of a whitish colour and of old date at the time of the autopsy. The cerebral arteries are not atheromatous or notably thickened.

The right hemisphere was flaccid, and sank down after the brain was taken out. The left hemisphere was firm, with flattened convolutions.

The heart is enlarged, and weighed 20 oz. The left ventricle, and the left auricle also, were much hypertrophied and dilated.

The aortic curtains are much thickened and fibrous, and con-

tracted, with cretaceous nodules in their substance. Their edges and ventricular surfaces are much eroded, especially the anterior curtain, the edge of which is deeply excavated, exposing a calcareous spicule in it. This and the right posterior curtain are perforated. There is a small excavation in the ventricular wall, about the size of a small pea, immediately beneath the junction of the posterior curtains, and close to the pin-hole perforation in the right posterior one. There were no fibrinous masses adherent to the valve, which was very incompetent when tested with water. The orifice is stenosed.

The mitral valve is much thickened also. The orifice admitted one finger only. On the edges of the curtain, and on the thickened chordæ tendineæ, are slightly raised and flattened fibrinous deposits.

The patient had been a sailor, then a stevedore, and lately a brewer's labourer. He had taken a good deal of beer and also spirits. Eighteen years before he had had rheumatic fever in India; no other illnesses. His wife had had seven children, who all died young, and one miscarriage. His father died of a paralytic stroke. The family history is otherwise good.

He was apparently quite well up to the time of the hemiplegic attack, when he was taken with severe headache and loss of power in his legs, and staggered and fell, striking his face against a dray. He had been working in a hot place, and the attack came on when he came out into the yard.

He had complete motor paralysis on the left side with loss of sensation, and loss of control over the evacuations. Sensation and some motor power were recovered in the leg; but there was little improvement in the arm and no voluntary control of the sphincters, and he continued to complain of headache.

There was evidence of enlargement of the heart, and of some increased dilatation after admission. A loud to-and-fro bruit was heard over the aortic valves, and a systolic murmur at the apex.

There was a small quantity of albumen, with some epithelial and granular casts, in the urine, which was of normal reaction and specific gravity.

The night and morning temperature chart showed a slight degree of pyrexia, 98°—100·6° for four days after admission, and a temporary elevation at intervals subsequently. The fatal seizure came on quite suddenly in the afternoon, and he quickly became comatose and died.

At the autopsy, in addition to the lesions of heart and brain above described, the spleen was found enlarged, weighing 18 oz., it was fleshy, not softened, and contained no "infarcts." The kidneys weighed 15 oz.; on the convex border of each was a depressed cicatrix, but no recent "infarcts." The lungs were œdematous and congested, and somewhat consolidated posteriorly, with slightly granular section. The aorta was slightly atheromatous.

The specimens are, I think, of interest:

1. As exhibiting concurrently cerebral lesion, more and less commonly observed in association with endocarditis, and associated with, and indicative of, a less and greater degree of virulence in the character of the cardiac lesion, with which they are respectively related.

2. As presenting features bearing upon the question as to the nature of the relation of cerebral hæmorrhage to the endocarditis with which it is sometimes associated; whether this occurs, when not dependent upon arterial degeneration, from rupture of an aneurysm resulting from septic embolism, according to the views expressed by Dr. Goodhart, and supported by some cases recorded in vol. xxviii of the 'Transactions,' which were adduced as evidence of the origination of aneurysm from septic emboli; or whether it is more commonly independent of embolism, resulting from a lesion of the vessels at the seat of hæmorrhage, through septic infection of the thrombus formed in consequence of such lesion.

In vol. xxviii of the 'Transactions' of this Society Dr. Goodhart has recorded three cases of hæmorrhage into the substance of the brain associated with acute endocarditis in young subjects, which he had met with in a period of six months at Guy's Hospital. But it would appear that such an experience is quite exceptional, and that this complication of endocarditis is really a rare one.

Thus Osler in his Gulstonian Lectures for 1885, on "Acute Endocarditis," mentions embolic softening of the brain, simple or purulent, as exceedingly common in that disease, and hæmorrhage on the surface of the brain as having been twice seen by him in endocarditis; but does not mention intra-cerebral hæmorrhage in connection with it. Rosenstein, in 'Ziemssen's Cyclopedia,' observes that extravasations into the meninges have been repeatedly observed in endocarditis, sometimes confined to the surface, at other times piercing deeper, occasionally into the cerebral substance itself.

I refer to this last statement, because I think that a consideration of the facts in Goodhart's cases leads to the conclusion that in all three of them the intra-cerebral extravasation occurred from meningeal branches of the middle cerebral artery; the blood being effused deep down in sulci, and escaping, in the direction of least resistance, through the cortex into the white substance of the hemisphere. In each case the clot was outside the central ganglia, and had an intimate relation with some particular spot at the surface of the brain. Thus, in his first case the seat of hæmorrhage was indicated by a softened spot in the Sylvian fissure; in the second case an aneurysm (?) was found in the insula; in the third case the blood had burst through to the surface. And I think this may have been so in my case also, where the clot was similarly situated. I think, then, that these more exceptional cases of *intra-cerebral* hæmorrhage associated with endocarditis may have been *meningeal* in their source, like the extravasations of blood upon the surface of the brain which are more frequently found in that disease, the difference being more apparent than real, as Rosenstein implies.

As regards the pathology of cerebral hæmorrhage occurring in association with acute endocarditis, according to Dr. Goodhart's conclusion from the cases which he brought forward in the communication above referred to, it is attributable to *septic embolism* of branches of the cerebral arteries leading to the formation, and subsequently to the rupture, of aneurysms, or aneurysmal dilatations, of them by softening of their walls.

In the present case, the fact that the plugging of the trunk of the right middle cerebral artery, which was almost certainly embolic, led only to white softening of the brain substance, would indicate that the endocardial lesion had not, at the time of that occurrence, the destructive character exhibited in the specimen; and the subsequent hæmorrhage might have been brought about from the lodgment of a smaller and more virulently infective embolus in a deeply-placed *meningeal* branch of the left middle cerebral (without any notable clinical symptoms), leading to the formation of an aneurysmal dilatation of it, and ultimately to hæmorrhage by rupture of the aneurysm.

But it is possible that the hæmorrhage may have been brought about in this, and in Dr. Goodhart's case also, not by *embolism* (with, or without, the formation of a true aneurysm), but by

thrombosis of the vessel, owing to some lesion of its inner walls, and subsequent softening and rupture of it from infection of the thrombus by streptococci or staphylococci, washed off the ulcerated aortic curtains, or discharged from an abscess formed in the ventricular wall in the position of the excavation seen immediately below the valve.

To slight lesions of the endothelial surface from too great distension, must, I think, be attributed the occurrence of adherent *antemortem* coagula in dilated cardiac cavities, of spontaneously occurring thromboses of veins and arteries, and infarcts often found in the absence of any ostensible source of embola.

To the formation, and septic infection of a thrombus upon a superficially abraded, or otherwise injured, spot of the endocardium, with subsequent softening of it, and of the ventricular wall beneath it, is attributable the excavation seen in the ventricular wall, which would in time have led to perforation.

It seems probable that in these patients suffering from ulcerative endocarditis, the combined effects of septicæmia impairing the nutrition and resistance of the vessel, and of hypertrophy of the left ventricle and albuminuria, tending to increase the strain upon them, may have led to a lesion of the endothelial lining of certain branches of the cerebral arteries, and to their subsequent rupture through septic infection and softening, first of the protective thrombus covering the injured spot, and then of the damaged arterial wall itself.

Such cases as this and those adduced by Dr. Goodhart, prove the occurrence of cerebral hæmorrhage secondarily to ulcerative endocarditis; but there is nothing in this case, nor, as I think, in the facts recorded in Dr. Goodhart's cases, to warrant the conclusion, either that the cerebral hæmorrhage in these cases was due to embolism with the formation and subsequent rupture of an aneurysm resulting therefrom, or that cerebral hæmorrhage associated with endocarditis, is commonly so caused.

In Goodhart's first case, that of a youth, aged 18, to which he attached more especial weight, there was definite clinical evidence of embolism of one brachial artery, there was an aneurysmal pouch on one middle cerebral artery, and aneursymal dilatation of the other, and a fatal cerebral hæmorrhage. But, as regards the evidence of the dependence of the hæmorrhage on embolism and aneurysm, it may be objected—

(1) That where there was definite evidence of the occurrence of embolism (at bifurcation of the brachial artery), the autopsy showed that the artery was occupied by a suppurating thrombus, but no aneurysm and no hæmorrhage.

(2) That where the autopsy showed an aneurysm on one middle cerebral artery, its situation on one side of the vessel, and the absence of a previous hemiplegic attack, exclude the idea of embolism; and no hæmorrhage had occurred.

(3) That at the seat of hæmorrhage there was no evidence of embolism, or aneurysm.

In his third case, also a youth, aged 19, there was old and recent hæmorrhage in the left hemisphere, and an aneurysmal pouch on one posterior cerebral artery. But the situation of the latter, "not at a fork in the vessel," was not indicative of embolic origin, and it had not given rise to hæmorrhage; and at the seat of hæmorrhage, no evidence of aneurysm or of previous embolism was discoverable; and the autopsy showed that the hemiplegic attack, which was the first clinical symptom of cerebral lesion, was due to hæmorrhage.

In the second case, there had been an hemiplegic attack without loss of consciousness, attributed to embolism, and the hæmorrhage was traced to what appeared to be an aneurysm of the left middle cerebral artery in the insula. But there was no plugging of the trunk of the left middle cerebral artery, and the hemiplegia appeared to have been due to hæmorrhage, a large part of the clot being of older date; and it appears doubtful whether the "aneurysm" was a true one, or only a cavity formed by extravasation of blood into the adventitious coat, or perivascular sheath of the vessel.

The evidence afforded by these cases as to the dependence of the vascular lesions associated with endocarditis on embolism, and as to the occurrence of cerebral or meningeal hæmorrhage in endocarditis by the rupture of aneurysms of branches of the cerebral arteries, formed as the result of (septic) embolism of them, appear scarcely sufficient to warrant Dr. Goodhart's positive inference from them.

The scanty occurrence of "infarcts"—or thrombotic necrosis—in spleen and kidneys, and their not infrequent absence from these organs, as in the present case and in Dr. Goodhart's third case, in the presence of valves covered with fibrinous "vegeta-

tions," and the presence of these thrombotic lesions, on the other hand, where there are no such valvular thrombi; and, lastly, their very unequal distribution in cases where many are found (as *e.g.* in Dr. Goodhart's first case, in which there were many infarcts in the spleen, but none in the kidneys), are facts opposed to the view that these arterial thromboses are generally, or mainly, due to embolism.

They seem to indicate a local factor as of chief importance in determining their occurrence, and a more complex pathogeny.

December 1*st*, 1891.

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4. *Case of ulcerative endocarditis affecting the pulmonary valves.*

By Arnold Chaplin, M.B.

This specimen was taken from a patient under the care of Dr. Sainsbury at Victoria Park Chest Hospital. The patient was a girl, aged 19, admitted for anæmia, she complained of great breathlessness, and on auscultating the heart a double murmur was heard at the base over the pulmonary artery. These murmurs frequently became altered and at times entirely disappeared.

At the necropsy the heart was not much enlarged, but on slitting up the pulmonary artery there was a small vegetation attached to the valve, and extending from this into the pulmonary artery was a large thrombus firmly adherent to the walls of the artery and filling it. On separating the vegetations from the walls of the artery, the inner coat of the vessel could be seen to be eroded. There were small vegetations on the aortic and mitral valves. The lungs contained traces of infarcts at both bases, but there were none in the spleen or kidneys. *January* 19*th*, 1892.

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5. *Two hearts showing tricuspid stenosis in association with mitral stenosis.*

By Arnold Chaplin, M.B.

The first of these specimens was taken from a case under the care of Dr. Harrington Sainsbury at Victoria Park Chest Hospital. The patient, a girl aged 18, was admitted into the hospital complaining of great shortness of breath and swelling of the legs. On admission the lips, cheeks, and fingers were blue. There was considerable œdema of the legs. The pulse was 132 and the respirations 38. The heart's apex beat was a quarter of an inch outside nipple line, and the cardiac dulness extended two finger's breadths to right of the sternum. At the apex could be heard a presystolic murmur and a faint systolic murmur. The patient died eight days after admission, having had previous to death an attack of hæmoptysis. The patient had never had rheumatic fever, but had gone through an attack of scarlet fever eleven years ago. At the necropsy the mitral valve was stenosed to an extreme degree, and the tricuspid valve scarcely less so. The aorta was diminished in size.

As to the cause of this condition, three possible explanations were given. (1) The mitral orifice was stenosed as the result of some rheumatic attack, and the tricuspid disease was secondary to the mitral. (2) The tricuspid disease was due to congenital causes, and the mitral due to causes arising after birth. (3) Both tricuspid and mitral disease were due to congenital causes. Taking into consideration the stenosis of the aorta, the small size of the heart generally, and the extreme stenosis of the tricuspid valve, it was submitted that the tricuspid disease was due to congenital defect, and the mitral possibly to causes arising after birth.

In the other heart the pathology was much clearer. There was a distinct history of rheumatic fever. At the necropsy the mitral orifice was stenosed to an extreme degree, and the tricuspid opening was narrowed so as only to admit the tips of two fingers. Here clearly the cause was in the first instance the mitral stenosis, the tricuspid disease being secondary *May 3rd*, 1892.

6. *Secondary epitheliomatous growth in the heart.* (*Card specimen.*)

By H. D. Rolleston, M.D.

Microscopic sections showing a squamous-celled epitheliomatous growth in the heart muscle were shown.

From a man who was found dead in the street. At the *post-mortem* his penis was found to have been amputated in the past—presumably for epithelioma. The only other morbid condition found was a mass of new growth in the apex of the heart, which was found to be a squamous-celled epithelioma.

November 3rd, 1891.

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7. *Malformed heart with an undivided auriculo-ventricular aperture, and a left superior vena cava.* (*Card specimen.*)

By F. C. Turner, M.D.

The specimen, which was obtained from an infant aged 14 months, shows a single auriculo-ventricular aperture, and imperfection both of the interauricular and interventricular septa, with free communication between all the four chambers of the heart. The aperture is guarded by four curtains; a large anterior or infundibular curtain, corresponding with the greater mitral flap and infundibular flap of the tricuspid, and extending over the incomplete septum inferius; and three smaller parietal curtains, two in the right and one in the left ventricle. The aorta and pulmonary artery are normally formed, and the septum aorticum is united with the septum inferius. The septum superius appears to have been fairly developed and presents a still open foramen ovale. The Eustachian valve is also well formed. The inferior and right superior vena cavæ enter the right auricle in a normal manner. The coronary sinus is very wide, and is continuous with a left

superior vena cava, which descends in front of the pulmonary artery and left auricle, just to the left of the auricular appendage. The pulmonary veins of each side enter the left auricle, which is small.

The right auricle is large, and was distended with blood-clot. The right ventricle appears to be more muscular than the left, but the latter cavity is the more expanded, and formed the apex of the heart.

The organ was much enlarged and very broad, displacing the anterior borders of the lungs outwards.

The child died from broncho-pneumonia. *January 19th*, 1892.

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8. *Congenital malformation of heart.*

By Norman Moore, M.D.

The heart of a boy aged 5 months, a patient under Dr. Norman Moore's care at St. Bartholomew's Hospital from the age of three weeks. The aortic arch is somewhat disproportionately large, and arises from an abnormally large and thick left ventricle. A mitral valve with a partial third flap opens into the left ventricle from a left auricle of about normal size. The mitral flap bears the normal relation to the aortic valves, which are also normal. The foramen ovale is open, and the right auricle is of double the normal capacity and thickness. There is no true tricuspid valve, but only an opening the size of a common pin, which leads into a right ventricle not larger than two pins' heads. This has no communication with the left ventricle. A minute pulmonary artery without valves issues from the right ventricle. This pulmonary artery grows much wider as it approaches the ductus arteriosus, which is patent and nearly as wide as the pulmonary artery at its widest part.

The circulation was chiefly if not entirely carried on by the single ventricle, the pulmonary blood-stream being directed through the ductus arteriosus from the aorta. The blood from the hypertrophied right auricle was driven into the left auricle, and thence, mixed with the aërated blood from the lungs, went through

the wide mitral orifice into the left ventricle. There was no unmixed blood current. The arteries given off from the arch of the aorta were normal. The other viscera of the chest and abdomen showed no abnormality. The child was cyanosed, sometimes deeply, sometimes only slightly. It had no clubbing of the fingers, toes, or nose. It was always very short of breath, its respirations being usually about 60 per minute. Its pulse varied from 160 to 180. It never sucked very well. A first and second heart-sounds were audible. I observed the physical signs first on August 29th, 1891, and afterwards on September 2nd, 5th, 9th, 12th, 19th, 26th; October 3rd, 10th, 24th; November 7th, 15th, 21st, 28th; December 5th, 12th, 19th; but never heard any murmur. The general character of the sounds approached that of the fœtal heart. A few purpuric spots appeared on the child's skin. It was very irritable. The ultimate cause of death was pulmonary catarrh.

February 2nd, 1892.

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9. *Congenital heart disease; pulmonary stenosis; patent septum ventriculorum.* (*Card specimen.*)

By H. D. Rolleston, M.D.

The heart weighed 20 oz. The right auricle was both dilated and hypertrophied. The tricuspid valve was thickened. The right ventricle was hypertrophied, so as to resemble the left ventricle, and somewhat dilated. The pulmonary valves were welded together so as to form a funnel projecting up into the small thin-walled pulmonary artery.

The left auricle was normal and the fossa ovalis intact. The mitral valve was thickened and the left ventricle hypertrophied, but of about equal thickness with the right. The inter-ventricular septum in the situation of the "undefended space" is patent. The circumference of this communication between the ventricles is $2\frac{7}{8}$ inches, and its edges are rounded.

The aortic orifice is directly over the septum, and that vessel may thus be said to arise from both ventricles. The aortic valves

are somewhat thickened. The ductus arteriosus is obliterated and small.

W. P—, aged 20 years, was always blue, but was considered to be fairly strong till puberty. At the age of 17 years he had two slight attacks of rheumatism, and became of a deeper blue colour, and suffered from dyspnœa.

He was an in-patient in 1888 in St. George's Hospital, and several times subsequently, under Dr. Dickinson. He was very cyanosed and had very bulbous fingers. A systolic murmur was audible all over the cardiac area, somewhat variable from time to time, but loudest over fourth interspace to left of sternum. No thrill was ever felt. Death from hæmoptysis, from phthisis.

This condition, viz. pulmonary stenosis with patency of the septum ventriculorum, is one of the commonest varieties of congenital morbus cordis. This case is brought forward in order to draw attention to a possible connection between the presence of a thrill over the pulmonary artery and the nature of the lesion giving rise to it.

In cases of complete obliteration of the pulmonary artery with extensive communication between the right and left sides of the heart, the fluid vein produced is often not of sufficient intensity to produce a murmur and hardly ever a thrill.

Now, in a case of pulmonary stenosis with a patent septum to the ventricles, the fluid vein produced at the pulmonary orifice will not be so powerful as in the case of pulmonary stenosis with a closed foramen ovale and intact septum to the ventricles, and a hypertrophied right ventricle. As a thrill is the expression of a fluid vein of considerable intensity, while a murmur is produced by a less powerful eddy in the blood stream, it is not unreasonable to expect to find pulmonary stenosis with an intact septum ventriculorum indicated during life by a harsh systolic murmur and a systolic thrill over the pulmonary artery, while pulmonary stenosis with a patent septum to the ventricles would be accompanied by a systolic murmur without any thrill, the systolic murmur being over the cardiac area and not especially over the pulmonary artery.

This case agrees with this hypothesis. In looking through the records of published cases, however, I have found some which directly contradict, while others support this *a priori* of suggestion. Owing to the fact that no definite statement as to the absence of a

thrill is made in a large number of the cases, I have not sufficient material at present, to draw up a satisfactory tabular statement as to whether the presence of a systolic thrill, and murmur over the pulmonary artery may, with any degree of probability, indicate pulmonary stenosis associated with an intact septum ventriculorum.

November 3rd, 1891.

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10. *A case of patent ventricular septum, together with an aneurysm of the base of the aorta opening into the right ventricle.*

By W. Hale White, M.D.

John D—, aged 15, was admitted into Guy's Hospital, January 25th, 1892, for shortness of breath. He works as a gardener's boy. He had measles as a child; he has never had rheumatic fever. During last summer he was well and active enough to play cricket. Three or four months ago he was suddenly taken ill with cough and cold (this was probably influenza, as there was much about at the time). Since then his feet and abdomen have swollen, and latterly his eyelids also, and he has become very short of breath.

On admission.—He has some scars on the back, which he attributes to an attack of shingles some time ago. There is slight general œdema; the cheeks are flushed. Pulse 136, small, compressible, regular. Over the whole præcordial area there is visible an almost continuous vibratory condition, both systolic and diastolic. The cardiac dulness extends upwards to the upper border of the third rib, to the left just beyond the nipple, to the right just beyond the right border of the sternum. Over the whole of the front of the chest there is a very loud rasping to-and-fro sound, closely simulating a pericardial rub. The point of maximum intensity is over the sternum opposite the third intercostal space. In front the murmurs do not seem to be conducted in any particular direction. Behind they can be easily heard, but are especially loud at the left apex. Some râles can be heard in the chest. Some albumen is present in the urine, and the liver can be felt

well below the ribs. For a time the lungs improved, but ultimately the signs of backward pressure increased; he developed a patch of pneumonia at the right base, and died April 2nd, 1892. The cardiac physical signs remained the same during the whole of his illness.

Post-mortem.—The lungs, liver, and kidneys showed the usual signs of backward pressure. There was some pneumonia at the base of the right lung.

The heart weighed 7½ oz. The right ventricle was dilated, but the left still more markedly; neither were hypertrophied. The pulmonary artery, the pulmonary valves, the tricuspid valve, and the mitral valve were all normal. The septum ventriculorum was deficient immediately below the right part of the anterior aortic valve, leaving an oval aperture large enough to admit a No. 10 catheter. The margin of this opening was thickened, but the septum for three quarters of an inch round it was very thin and semitransparent. The aortic valve directly above this aperture was a little thickened, but the aortic valves appeared competent. The sinus of Valsalva immediately above this valve was dilated into a thin-walled pouch, which bulged for three quarters of an inch into the right ventricle; at the bottom of this pouch was an aperture which would admit a No. 10 catheter; this was probably due to the bursting of the pouch into the right ventricle. Opposite this aperture in the pouch, on the right wall of the right ventricle the lining membrane was thickened and opaque, apparently because blood passing from the aorta to the right ventricle impinged on this spot. There was another similar patch on the septum between the ventricles and in the right ventricle, apparently due to the passage of blood from the left to the right ventricle.

It appeared probable that the whole of the upper part of the septum between the right ventricle on the one hand, and the left ventricle and lower part of the aorta on the other, was congenitally deficient in thickness, and that at the upper part of the septum ventriculorum this had led to a failure of complete closure, and hence the aperture of communication between the two ventricles. This weakness had also led to the formation of a small aneurysm behind the right anterior aortic valve, and this had, when the boy first complained of symptoms, ruptured into the right ventricle. It will be noticed that the aperture of communication between the two ventricles is not in the usual place of the aperture of a patent

septum, but rather to the right of it. A very similar case was shown at this Society at the last meeting by Mr. W. H. Tate.

May 17th, 1892.

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11. *Case of malformation of the heart.*

By W. W. H. Tate, M.B.

Patient, aged 22, a waiter, was admitted to University College Hospital in January last under the care of Dr. Poore, to whom I am indebted for permission to show the present specimen. Patient was suffering from pneumonia affecting the right side, and on examining the heart a systolic thrill was felt at the apex, and a systolic and diastolic bruits were heard over the cardiac area. The inflammation gradually extended, and patient died four days after admission.

No previous history of rheumatism or of any cyanosis.

At the autopsy, in addition to the ordinary signs of pneumonia, a trumpet-shaped tube of membrane was found projecting into the right ventricle, at the junction of the attached margin of the septal and infundibular segments of the tricuspid valve. On passing a probe along this hollow membranous tube it was seen to communicate by a rounded opening with the lower part of the anterior cusp of the aortic valve. The present condition appeared to have started as a saccular projection into the right ventricle from the left side of the heart at the undefended space, which later on became perforated.

I have been unable to find any similar case among the records of the Pathological Society for the last twenty years.

May 3rd, 1892.

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12. *Incomplete auricular septum with perfect closure of the foramen ovale.* (*Card specimen.*)

By HERBERT P. HAWKINS, M.B.

FROM a boy, aged 3, who was admitted into St. Thomas's Hospital on April 21st, 1892, suffering from papilloma of the larynx, and died within two hours of admission during the performance of tracheotomy.

Post-mortem.—The auricular septum of the heart was found to be imperfect in its lower part, so that the auricles communicated by a circular aperture, with a diameter of half an inch, and smooth, rounded edges. Immediately above this aperture the perfectly closed foramen ovale could be plainly seen.

The endocardium of the auricles was somewhat thickened, but there was no obvious alteration in size or wall-thickness of auricles or ventricles. There was no other malformation.

The liver and kidneys showed no signs of chronic congestion, and no symptoms seem to have resulted. (Cf. 'Path. Soc. Trans.,' vols. i, xix, and xxix, for similar cases.) *May 3rd*, 1892.

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13. *Bifid apex of the heart.* (*Card specimen.*)

By H. D. ROLLESTON, M.D.

THE specimen was removed from a woman, aged 40, who died with mitral and aortic obstruction. The heart weighed 15 oz. The apex of the heart is formed by the left ventricle. Projecting from the right side of the apex is a second apex, viz. that of the right ventricle. The right ventricle was not markedly hypertrophied or dilated.

The existence of a distinct apex to the right ventricle, in addition to that of the left side, is to be regarded as a persistent condition of the bifid condition met with at an early period of fœtal life.

December 1st, 1891.

14. *Case of aneurysm of the descending aorta bursting into the muscles of the neck.* (*Card specimen.*)

By Walter S. Lazarus-Barlow, M.B.

The patient, aged 32, was admitted to St. George's Hospital for a myeloid sarcoma of the femur. The limb was amputated, and the patient improved until six weeks after his admission, when he became restless and had difficulty of breathing. At the last he sat up in bed, cried out loudly, the neck became suddenly swollen, and he died choking.

At the autopsy blood was found extravasated on both sides of the neck among the superficial muscles from a large collection of blood-clot (recent) behind the pharynx, which had tracked up from the thoracic aorta. The mass behind the pharynx had greatly narrowed the lumen of the pharynx and the œsophagus, but had not burst into either the œsophagus or bronchi. The heart was normal.

In the posterior part of the descending part of the arch is an orifice leading into a thin-walled saccular aneurysm the size of a tangerine orange; it lies behind the transverse part of the arch, and towards the left border gives off a thin-walled pouch; these two communicate with one another. Superiorly the aneurysm has burst, and is in free communication with a false aneurysm full of blood-clot, which is practically limited by the deeper layers of the deep cervical fascia. There was no erosion of the vertebræ, nor evidence of any secondary sarcomatous deposit.

I have not been able to discover a report of any similar case, nor is the possibility of such a termination even mentioned in the ordinary text-books. *May 17th*, 1892.

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15. *Aneurysm* (*?*) *of aorta in a child of four.*

By Edgar Willett.

The specimen shown consists of the heart, the arch of the aorta, the commencement of the great vessels of the neck, and the surrounding structures. The child was under the care of Dr.

Church. Unfortunately, the specimen was removed from the body by one of the post-mortem clerks, and has been cut in two, so that the two parts do not retain their exact relative positions. This has been rectified as nearly as possible. The aorta has been laid open along the greater curvature of the arch, and the great vessels have been similarly divided. At the commencement of the descending aorta there is a slightly irregular opening situated above and rather to the right of the first aortic branch. This leads into a sac, about the origin and nature of which there must be a good deal of uncertainty; in places its walls are thick and well formed, and are as thick as that of the aorta itself. Its exact relations, particularly its relation to the pulmonary artery, I have been unable to make out, owing to the unfortunate accident connected with its removal from the body, but whatever its origin, it is clear that it is a definite sac communicating with the aorta. A possible mode of origin is that from its situation it may be connected with the ductus arteriosus, which for some cause has become closed at its proximal end, and has remained open at its distal end, and has subsequently become distended. Another theory is that it is the remains of an enlarged lymphatic gland, which has broken down and has discharged its contents into the general blood-current; of the two I think this to have been the more likely. Microscopical examination of the wall of the sac shows no elastic tissue, and very little, if any, unstriped muscular tissue. It resembles coagulated fibrin or old blood-clot more than a true wall; there is an attempt at a lining membrane.

The heart itself shows very clearly the signs of recent pericarditis from which the child died.

The sac contained some recent (*post-mortem*) blood-clot, with some laminated clot on its walls. History as follows:

Robert J—, aged 4, admitted November 9th, 1891.

History.—Was quite well and at school three days ago. Came home in the afternoon and complained of feeling tired. Face then noticed to be rather puffy. Slept well that night and took his food well. The next morning his face was much swollen, and he complained of headache; no sickness. Next evening seemed worse, and was light-headed, with visual hallucinations. Swelling of face increased. Urine noticed to be thick since onset of symptoms.

Past history.—Cough for two months; never scarlet fever or diphtheria, and no illness in house.

Family history.—Father, aged 47, suffers from rheumatic gout. Mother, aged 40, healthy. Three sisters well; one died young.

Present condition.—Well nourished; face very puffy, eyelids much swollen; conjunctivæ œdematous and watery. Nose running. Tongue: slight red fur. Pulse 152, good volume, slightly increased tension. Resp. 44, laboured. Temp. 101·6°. Bowels open this morning. An eruption of herpes on lips has appeared since admission.

Chest.—Well shaped and well covered. Movements equal. Percussion note much impaired over left front of chest, normal behind. Bronchial breathing and crepitations heard at right (?) apex in front, and also faintly behind. A few moist sounds all over back.

Heart.—Apex beat, fifth space inside nipple line. A systolic murmur heard all over cardiac area, most loudly at apex.

Abdomen.—Protuberant, resonant all over. Lumbar œdema marked.

Legs.—Œdematous.

Urine.—Heavy cloud of albumen and some blood.

November 10th.—Fair night, but breathing distressed; otherwise as before. Moist sounds increased.

11th.—Slept fairly; takes food well; sick this morning. Temperature lower. Less puffy.

14th.—Better.

About the same, with slight improvement, but some whooping-cough till 25th.

27th.—Not so well; does not sleep or take food so well.

28th.—Temperature still up at night (102° F.). Much impairment, almost amounting to absolute dulness, over left front of chest.

30th.—Pericardial friction.

December 3rd.—Pericardial friction less; breathing more laboured. Died at night.

Post-mortem.—Pericarditis. Collapse of lungs with broncho-pneumonia of left side. Parenchymatous nephritis.

April 5th, 1892.

16. *A specimen showing a communication between the left internal carotid artery and a dilated sphenoidal sinus.*

By J. Jackson Clarke, M.B.

The specimen, which is in the St. Mary's Hospital Museum, comprises the left half of a section of the fore part of the base of the skull and the nasal fossæ. The sphenoidal sinus is so greatly dilated that its lining membrane rests posteriorly on the cartilage which separates the basi-sphenoidal from the basi-occipital bones. Above, it is in contact with the dura mater at several points; the lateral expansion is also considerable. In front within the sinus are two small myxomatous polypi, which are attached respectively to the outer margins of the right and left openings into the nasal fossæ. In the recent state the sinus was completely filled with laminated clot, which was firmly attached at a point corresponding to the last bend of the internal carotid artery. At this point is a round perforation one eighth of an inch in diameter, leading into the carotid artery, which is firmly attached to the margins of the aperture. The carotid artery and the cavernous sinus appear to be normal, save for this communication. There are well-marked adenoid growths in the naso-pharynx.

The case is that of a boy, aged 13 years, who, twenty weeks before death, was admitted into St. Mary's with a compound fracture of the frontal bone on the left side. There was no epistaxis at this time. The boy did well, and at the end of a month left the hospital, and soon afterwards was seized with epistaxis, which ceased and recurred from time to time, increasing in severity. He was brought back to St. Mary's dying from profuse hæmorrhage.

At the autopsy I could trace the line of fracture across the left orbital plate, but in the body of the sphenoid I was not able to identify it on account of the thinning of that bone. I am of opinion that the case is one of fracture of the base crossing the body of the sphenoid, and causing a non-perforating injury to the left internal carotid artery, and later a minute aneurysm which opened into the sphenoidal sinus. The dilatation of the latter may have begun before the fracture occurred, but I have no doubt that the successive hæmorrhages and the presence of laminated clot increased the dilatation. *December 1st*, 1891.

17. *Aneurysm of internal carotid, occlusion of subclavian, and narrowing and thickening of other arteries, due to syphilis.*

By WALTER EDMUNDS, M.C.

CHARLES G—, aged 36, was admitted into St. Thomas's Hospital on November 6th, 1891, under the care of Sir William MacCormac, to whom I am indebted for permission to exhibit the specimen.

The patient was suffering from a pulsating tumour on the right side of the neck; this had been first noticed a month previously, and had since then increased rapidly in size. It caused no pain or discomfort; but a few days before admission the patient had been seized with a sudden attack of giddiness which caused him to fall; he, however, soon recovered.

The tumour is situated about the bifurcation of the right carotid; it pulsates forcibly and expands. Examination of the tumour sometimes causes an attack of giddiness or faintness.

There is no pulsation to be felt in any artery in either upper extremity; a loud murmur can be heard about the base of the heart. There is a history of a venereal affection twelve years ago, and two years ago of hair falling out and of large ulcers on the front of the chest; the scars of these ulcers are very evident, and the patient has undoubtedly had syphilis.

On account of the cerebral symptoms produced by the mere examination of the aneurysm and the presumably diseased state of the great arteries, no operation was undertaken. The patient died comatose twelve days after admission.

Post-mortem examination.—Body well nourished. Heart somewhat enlarged, the pericardium adherent, but the adhesions can be easily broken down; a rounded prominence two inches in diameter projected from the groove between the right auricular appendage and the pulmonary artery. On section this proved to be a gumma. The arch of the aorta is uniformly thickened, the thickening being greatest in the outer coat; the thickening extends along the innominate.

The second part of the right subclavian is also greatly thickened in its outer coat, and its lumen is so reduced as only to admit the passage of a bullet-probe; the right axillary, brachial, and radial arteries are small and thin-walled, but show no sign of disease.

The right common carotid is nearly normal. The right internal carotid has springing from it on its outer side close to its origin a globular aneurysm two and a half inches in diameter; beyond the origin of the aneurysm the internal carotid is normal; the external carotid was narrowed and adherent to the aneurysm.

The left common carotid is greatly narrowed at its origin from the aorta, only admitting a bullet-probe; it is lined by adherent clot. The left external and internal carotids are also narrowed.

The left subclavian is similarly narrowed at its origin, but at three quarters of an inch from the aorta it becomes completely impervious, ending in a fibrous cord.

The descending aorta is enormously thickened, the thickening being mainly in the outer coat (see below, Fig. 2). The abdominal aorta, the iliacs, and also the intra-cranial arteries are normal.

The liver, kidneys, and spleen are all enlarged, but show no sign of past syphilitic disease.

Transverse section of the commencement of the descending aorta shows how great the thickening is. The actual measurements in millimetres of this and of a normal aorta (for comparison) are as follows:

	Outer coat.	Middle coat.	Inner coat.	Total.
Normal aorta near valves .	0·05	1·1	0·08	1·23
Normal abdominal aorta near bifurcation . . .	0·1	0·75	0·2	1·05
Specimen at lower end of arch	3·2	4·63	1·13	8·96

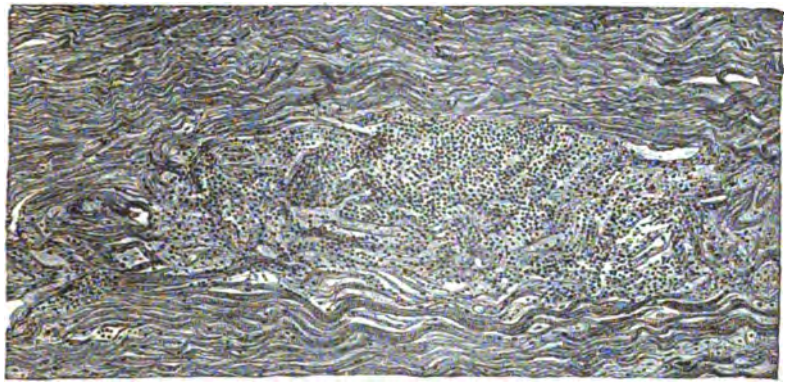
Thus the aorta wall is nearly eight times thicker than normal.

Microscopic examination shows the thickening to be in all the coats, and due partly to hypertrophy and partly to a gummatous infiltration of the wall (see Figs. 2 and 3).

FIG. 2.

Transverse section of descending aorta; the intima is at the lower end of the drawing (× 18). All three coats are greatly hypertrophied, but especially the middle, which in its outer part is the subject of a gummatous infiltration, seen more highly magnified in Fig. 3.

FIG. 3.



Part of section of aorta seen in Fig. 2, more highly magnified (× 100). It is from the outer part of the middle coat, and shows a small round-celled infiltration, doubtless gummatous.

Remarks.—Cases of obliteration of arteries from various causes are not unfrequently described. Joseph Hodgson, in his "Diseases of Arteries and Veins" (1815), relates a "case of obliteration of the brachial, radial, ulnar, femoral, popliteal, and femoral arteries." From rigors being a prominent symptom in the history of the case, and from its short duration, it seems probable that this was a case of ulcerative endocarditis with embolism. Savory, in the 39th volume of 'Transactions' of the Royal Medical and Chirurgical Society (1856), records a "case of a young woman in whom the main arteries of both upper extremities and of the left side of the neck were throughout completely obliterated." There had been no pulse at either wrist for about five years. The results of a *post-mortem* examination are carefully described (the right and left subclavians and the left carotid were completely obliterated), but the cause of the disease is not apparent.

With respect to the gumma in the wall of the heart, a specimen of "ruptured aneurysm of heart (syphilis)" was exhibited before the Society in 1887 by Dr. Goodhart for Mr. A. Withers Green, and in the 'Transactions' for 1891 will be found an account by Dr. Newton Pitt of a "gummatous infiltration of the muscular wall of the heart leading to aneurysmal pouching and rupture."

May 3rd, 1892.

18. *Case of general arteritis (pulmonary and systemic) in a child, possibly the result of congenital syphilis; death by infarction of lungs, thrombosis of renal arteries with uræmia, and cerebellar hæmorrhage.*

By Herbert P. Hawkins, M.B.

The patient, E. F—, a girl aged 11, from whom this aorta was obtained, was admitted into St. Thomas's Hospital under the care of Dr. Harley, suffering, as it was supposed, from acute nephritis. She died on March 2nd, 1892, after an illness of three weeks' duration.

At the *post-mortem* examination it was found that there was gross disease of nearly every artery in the body, and that this arterial disease was in itself the cause of death by means of secondary effects upon lungs, kidneys, and cerebellum.

The aorta showed grey translucent spots and patches, for the most part varying in size from a split pea to a patch passing halfway round the tube, and extending for an inch or more in a vertical direction. The patches were smooth or slightly corrugated; they were raised well above the surface and could be felt as well as seen. This condition extended from the aortic valve to the bifurcation of the aorta, and there were one or two similar spots on the aortic valve itself, and one even on the endocardium immediately below that valve.

For a distance of 3 inches above the bifurcation there was a narrowing of the artery, so great that the lumen at one spot scarcely admitted a bullet-probe. This narrowing was due partly to a continuous thickening of the intima over this area, but largely also to a contraction of the artery wall, the breadth of the opened artery being but half an inch.

Similar patches occurred in the common carotid and subclavian arteries on both sides without any narrowing; also in the left internal carotid as it entered the cranial cavity, and in the right internal carotid, involving also the origin of the middle cerebral.

There was similar disease throughout the pulmonary arterial system; grey raised spots commenced at the pulmonary valve, and

were found to be thickly distributed as far as the vessels could be opened up with scissors.

There was no gumma or scarring of the kidneys; the liver was somewhat enlarged, and, though it showed no actual disease or scarring, presented on its upper surface a patch of peritonitic thickening. The spleen had been at some time diseased; it was large, weighing 5 oz., its tissue was exceedingly hard, and its capsule thickened and surrounded by old peritonitic adhesions. The teeth showed no change.

As to the nature of the disease:—Microscopically the grey translucent patches in the aorta show a development of indistinct fibro-cellular tissue in the intima, with an accumulation of leucocytes here and there in both middle and outer coats, especially around the vessels. The new tissue is stable and shows no tendency to fatty or other degenerative change; but here and there upon the surface patches of deeply staining amorphous material are seen, representing necrotic remains of the superficial part of the intima. There is no deposit of clot on the diseased surface.

Looking at the age of the patient, at the wide distribution of the disease throughout systemic and pulmonary arteries, at the absence of primary renal disease, at the definite contraction of the abdominal aorta, and at the condition of the spleen, it is not improbable that the arterial disease is here a result of congenital syphilis, although the microscopical characters are not identical with those described under this head in 'Path. Soc. Trans.,' 1877.

As regards the secondary effects:

(*a*) The left lung showed early, but complete, pneumonic consolidation of the whole of the lower lobe, and in the solid part could be distinguished the outline of a hæmorrhagic infarct of considerable size. There was a smaller infarct in the upper lobe. The right lung showed similar consolidation of the hinder halves of both upper and lower lobes, the anterior parts being emphysematous. Here also in the solid tissue could be seen the outlines of two infarcts; a third one lay in the middle lobe.

(*b*) The renal arteries towards their entrance into the kidneys were completely closed by clot, which was red and recent in the centre, but white and old around the periphery. There was an old infarct in one; microscopically there was no appearance of nephritis.

(*c*) There was a hæmorrhage into each lateral lobe of the cerebellum, the clots having the size of a hazel-nut.

(*d*) The heart, of which the valves were competent, showed some dilatation and hypertrophy of the left ventricle, due doubtless to the obstruction presented by the contracted aorta.

Previous history of the patient.—She had been healthy for the first ten years of her life, with the exception of measles at the age of six, and two attacks of influenza. There was no history of syphilitic symptoms in infancy, but unfortunately special attention was not directed to this point.

History of the fatal illness.—The symptoms which she presented, though they were misunderstood during life, are fully explained by the pathological conditions above described.

In the summer of 1891 she had a week's illness, suffering from cough and pain in the left side, which are probably to be attributed to infarction of the lung. In January, 1892, similar symptoms came on, the pain being first in the left side, later in the right; the cough with blood-stained sputum persisted up to the end of the illness. On February 7th the mother noticed that her legs were very cold and somewhat swollen; and a few days later swelling of the face set in. She now became exceedingly ill, and was admitted into hospital on February 20th.

On admission.—The diagnosis of acute nephritis could hardly be avoided. There was slight puffiness of the lower eyelids and a little œdema of the shins; the urine was found to contain a fair trace of albumen but no blood or casts. There was impaired resonance over the base of the right lung with rhonchi here and there over both. The heart's apex was beating in the fifth space one inch outside the nipple-line, and both at base and apex the second sound was markedly reduplicated. The edge of the liver was felt at the level of the umbilicus; the spleen could not be felt.

On February 23rd tubular breathing appeared at both bases, and the respiration rose to 48 per minute though the temperature remained normal. In the preceding sixty hours she had only passed 3 oz. of urine, and the pulse was 102 and was exceedingly tense.

On February 25th it was found that the urine contained a little blood, but very little albumen. She had passed only 8 oz. in the previous forty-eight hours; and severe vomiting set in.

On February 26th the 8 oz. passed contained no blood or albu-

men, and yet the child was obviously dying of uræmic poisoning.

She died on March 2nd with delirium and Cheyne-Stokes breathing; resp. 54 per minute, pulse 114, of great tension. The temperature remained normal throughout. The urine increased gradually in amount (up to 20 oz. daily) in the last four days of the illness, though all the symptoms continued unchanged.

Of pathological interest is the blocking of the renal arteries, which is here seen to produce uræmia as surely as does blocking of the ureters. The fact that the urine gradually became more abundant towards the end of the illness, and also became free from blood and albumen, is probably to be attributed to the gradual coming into play of the supplementary blood-supply from the lumbar vessels. Clinically we have such an interesting group of symptoms, as partial suppression of urine, œdema of face and feet, with a normal or slightly albuminous urine. *May 3rd*, 1892.

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19. *Infarcts in the spleen associated with thrombosis of the splenic vein.*

By H. D. Rolleston, M.D.

The splenic vein is occluded with firm, adherent, decolourised clot; the superior and inferior mesenteric veins are also thrombosed. The superior mesenteric vein is canalised, the clot having softened down in the centre. There is softening clot in the internal and external iliac veins on the left side. The clot from the splenic vein has spread into the portal vein, but only occupies part of the lumen of that vessel. The clot in the superior mesenteric vein was the oldest, then that in the iliac veins, then that in the splenic vein, while that in the inferior mesenteric was apparently of quite recent origin.

The spleen weighed 36 oz., and presented under the capsule extensive anæmic infarcted areas separated from the rest of the splenic tissue by a congested zone. Microscopically, these infarcts were seen to be composed of splenic tissue in a state of coagulation

necrosis, with extravasated blood corpuscles between them and the rest of the organ.

The splenic artery is free from clot, and its branches transmit injection fairly well, so that there is no evidence of their being blocked. The whole of the spleen, except the infarcted areas, was injected with carmine, so the circulation, both venous and arterial, has been brought to a standstill in the infarcted regions.

The liver showed a slight degree of cirrhosis.

There were traces of old dysentery in the colon, the rectum was recently inflamed. The vermiform appendix was adherent to the right side of the colon, covered over with recent lymph, and a hard concretion was beginning to ulcerate out.

This case seems worth recording as the infarction seems to have been due to the complete thrombosis of the splenic vein. It would naturally have been expected that this thrombosis of the splenic vein would have produced not only anæmic infarction but an hæmorrhagic infarction, as in Litten's experiments of ligaturing the renal vein, inasmuch as the outlet of venous blood is thus prevented.

It is hard to say why, with complete thrombosis of the splenic vein, parts only of the spleen were in the condition of anæmic infarction.

The patient had been in India for six years; had had ague often and two slight attacks of dystentery. He had not had syphilis, and had been a temperate man.

On August 31st, 1891, he was admitted into St. George's Hospital under Dr. Ewart with very profuse hæmatemesis; the spleen at this time was enlarged. He recovered slowly and remained very anæmic, so as to suggest the possibility of leucocythemia; an examination of his blood, however, showed this not to be the case.

Early in October ascites somewhat suddenly developed, accompanied by signs of thrombosis in the left femoral vein. After paracentesis the ascites did not re-accumulate, but he died worn out by exhausting diarrhœa.

Since this case was shown to the Society I have met with another case of thrombosis of the splenic vein associated with anæmic infarcted areas in the spleen. The patient was a woman who had extensive carcinomatous growths in the peritoneum, secondary to a primary columnar-celled epithelioma of the cæcum.

January 19th, 1892.

20. *Rupture of spermatic veins.*

By W. G. Spencer, M.S.

The specimen exhibited is the right testis and spermatic cord of an infant, the epididymis and lower part of the cord having been surrounded and infiltrated with blood-clot. Microscopic specimens show, in addition, large spermatic veins in the midst of the mass. It was taken from a child, fourteen days old, who was brought to the Westminster Hospital with a tumour in the right scrotum. The affection had been noticed three days after, but the mother could not say whether it was present at, birth. The birth was normal, and there were no other indications of injury or of disease.

The swelling involved chiefly the back of the testis and the lower part of the cord. The skin over the swelling was adherent and bluish black in colour. Beyond the swelling the skin was normal without signs of bruising or of inflammation. On puncture it proved to be solid in consistence, some blackish fluid escaping.

Mr. Macnamara saw the case, and it was agreed that the disease appeared suspiciously like a melanotic sarcoma. On incision the surface of the section looked black, the testis and the cavity of the tunica vaginalis were healthy, and there was no sign of blood-clot in a cavity. The diagnosis of melanotic tumour seemed correct, and castration was performed which was followed by rapid healing. But on microscopic examination by Dr. Hebb, the tumour was found to have been due to an infiltration of the epididymis and cord by extravasated blood.

Concerning the exciting cause of this condition I have no evidence. Light is thrown upon the predisposing conditions by a paper of mine on the origin of varicocele in vol. xl of the Society's 'Transactions.' In it I described the large size of the veins which, at first belonging to the Wolffian body, are transferred later on to the less vascular testis. The veins accordingly tend to become relatively less in size and number by a process of atrophy, which affects the right more than the left side. But these veins are still relatively large and numerous at birth, as can be seen in the drawings appended to the paper. *February 2nd*, 1892.

III. DISEASES, ETC., OF THE ORGANS OF DIGESTION.

1. *Case of median harelip.*

By H. H. Clutton.

[With Plate II, figs. 2 and 3.]

A girl, aged 15, who has never been submitted to any operation, and who can be seen in the adjoining room, shows the following peculiarities: exactly in the middle line of the upper lip is a small notch or fissure, and corresponding to it in position is a cleft of the alveolus. The notch in the upper lip is very small, but it will be seen that the skin in the floor of this fissure is continued on the under surface of the lip to the cleft in the jaw and so on into the nose. A drawing which I have had made shows this peculiar feature very well (see Plate II, figs. 2 and 3). On each side of this groove is a bridle or frenum attaching the under surface of the lip to each half of the upper jaw. There are, therefore, two frena in place of one ordinarily existing.

The cleft in the alveolus of the upper jaw is exactly central, as if the premaxilla were absent or divided. The palate is also cleft from one end to the other, but the margins in front are in contact. The vomer appears to be absent or rudimentary, not reaching the palate at any part.

There are no central incisors, but there is a lateral incisor and a canine on each side, and on the right there is also a swelling as if another tooth would shortly appear.

No operation has at any time been performed, but fifteen months ago three teeth were extracted by Sequah from the front of the jaw. Their exact nature cannot, therefore, be ascertained.

DESCRIPTION OF PLATE II.

Fig. 1 illustrating Mr. Shattock's specimen of Parepididymal Cyst. (Page 107.)

From a drawing by the author.

The spermatic vessels cross the posterior and inner surface of the cyst to reach the hilum testis, and are shown divided above and below by the removal of a part of the cyst-wall.

The vas deferens lies along the back of the cyst, and terminates in a normal epididymis; its divided upper end is marked by a bristle.

A normal hydatid of Morgagni projects into the sac of the tunica vaginalis which is quite distinct from the cyst behind the testicle.

Figs. 2 and 3 illustrating Mr. Clutton's case of Median Harelip in a girl aged 15 years, who had never been submitted to any operation. She had had three teeth extracted from the front of the jaw. (Page 52.)

In Fig. 3 the cleft lip is turned upwards to show the median fissure in the upper jaw.

Fig. 3.

S. G. Shattock del.

It is difficult to speak positively as to the correct explanation of this rare condition. Either the premaxilla is entirely absent, or the two globular processes of His, which ordinarily fuse to form the premaxilla, have partially failed to do so, although the lateral lobes have joined on each side.

Mr. Sutton, in his interesting lectures on Evolution in Pathology at the College of Surgeons in 1888, exhibited a dissected specimen of median harelip in the human subject. The premaxilla and ethmo-vomerine plate were absent. This would appea r,according to Mr. Sutton, to be the usual abnormality in man where a median harelip exists. But in some mammals, especially Rodents, the globular processes do not fuse, but remain permanently separate. Mr. Sutton gives illustration to prove that this is constant in some animals, and that in some of the marsupial embryos it may always be found.

Mr. Pitts showed a case of median harelip at the Medical Society in 1889, in which the cleft in the upper lip was quite median, extending half way to the nose. The premaxilla was centrally grooved, but the bone was otherwise perfect and there was no cleft in the palate. We thus have evidence recorded in recent years of two conditions in the human subject, causing a median harelip—one in which the premaxilla is absent, and the other in which the premaxilla is grooved in its central line.

The question arises as to whether, in the case recorded to-night, we are to ascribe this deformity to an absence of the premaxilla, or to a want of union between the two halves of the premaxilla. I am inclined to think that the premaxilla is present but ununited.

October 20th, 1891.

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2. *Two cases of tubercular ulcer of the tongue.*

By Charles A. Morton.

Since 1882 and 1883, when several cases of tubercular ulcer of the tongue were brought before the Society for the first time —when, in fact, the disease began to be generally recognised by surgeons in this country—there have been few cases recorded.

These cases were presented before it had become the habit to search for the tubercle bacilli as a sign of the tubercular nature of the disease. However, in 1884 Dr. Percy Kidd and Mr. Taylor exhibited microscopic sections of the disease, and in these cases bacilli were demonstrated, as Mr. Watson Cheyne had done in Mr. Godlee's case in the former series.

As now no specimen has been shown for six years, I have ventured to bring two before you this evening. For permission to bring forward the first case I am indebted to Mr. Penny, under whose care the patient was admitted into the Bristol General Hospital.

My *post-mortem* notes of the case are as follows:

Tongue.—Extending from the frenum to the tip is a narrow ulcer of about ⅓ inch in length, from before backwards, with a nodular edge, but fairly smooth base. Only at one spot was it indurated, and that was at a portion of the edge. The base was not indurated, nor was there any new growth, only ulceration.

The submaxillary glands on both sides were enlarged, and either caseous or contained caseating spots.

The lungs were full of miliary tubercles, and there were several caseous masses in each, and a cavity of large size at the left apex.

In the larynx there was extensive subglottic ulceration, and small ulcers on the outer surface of the arytenoids, the tops of which were also ulcerated, and they were swollen.

There were several miliary tubercles in one kidney, and one in the other. None were seen in the liver or spleen.

One epididymis was considerably enlarged and breaking down into purulent cavities. This testicle was quite healthy, though there was about half an ounce of clear serum in the tunica vaginalis. The other epididymis was quite healthy.

Microscopic sections were made from a portion of tissue which included the whole breadth of the base of the ulcer. An examination of these shows the base and surrounding tissue beneath the mucous membrane infiltrated with small round cells, amongst which are scattered numerous giant-cells. This infiltration, together with the giant-cells, extends for half an inch below the surface of the ulcer, showing the need of free removal in these cases, even when there is no induration.

The giant-cells are just scattered here and there in the mass of small round cells, and are not surrounded by epithelioid cells, but

in parts of the section the cells form round masses, in which are one or many giant-cells. Fragments of muscle are seen amongst the small-celled infiltration, not wholly destroyed.

At one edge of the ulcer, where the surface is slightly raised—probably forming one of the nodules mentioned in the naked-eye description—there is an ingrowth of surface epithelium such as occurs in an epithelioma.

The giant-cells have their nuclei arranged around the margin, or at one end of the cell, and in many, tubercle bacilli are to be seen—sometimes as many as a dozen are seen in one giant-cell. These bacilli are also seen amongst the small round-celled infiltration.

This ulceration of the tongue occurred in a man of fifty-five, and was of six months' duration. At one time the ulcer had almost healed and had then, as invariably happens, broken down again.

Before it began to heal there was much difficulty in the diagnosis from epithelioma; but the way in which little ulcers about the size of a pin's head formed and coalesced, strongly suggested tubercle. There is no clinical record when the pulmonary disease was first revealed by physical signs, but looking at the *post-mortem* appearances of the lungs, I should be inclined to think the pulmonary affection had preceded the other. The front incisor teeth were so rough that they were removed, so that probably there had been some abrasion of the tongue, and this had become inoculated with the bacillary sputum. There is, however, another possible way, in which the tubercular ulcer may have caused the pulmonary lesion. There were ulcerations of the pharyngeal aspect of the arytenoids, and possibly the infected sputum may have started the disease through being swallowed, and the disease may then have spread into the interior of the larynx and lungs.

I do not think the inspired air would take up bacilli from the *moist* secretions in the mouth. Even with the mouth open in sleep, I hardly think it would be dry enough.

CASE 2.—Knowing that I was about to show a specimen of tubercular ulcer of the tongue at a meeting of the Society, I was kindly invited to see a patient at the Bristol Royal Infirmary, under the care of Mr. Munro Smith, who was suspected by some to be suffering from this disease, by others to have an epitheliomatous ulcer. After excision Mr. Smith kindly presented me with the specimen to examine and bring here this evening.

The microscopic examination confirms the diagnosis. The appearances are practically the same as those just described, in connection with the other case, except that the bacilli have been more difficult to find. I have only found three bacilli in ten sections, each bacillus in the centre of a giant-cell. In sections of this ulcer, as in the other, there is a slight ingrowth of the epithelium at one edge of the ulcer, but to a much slighter degree than occurs in an epithelioma. In this ulcer we may observe tubercles scattered amongst healthy-looking glands and muscles, in a way not to be seen in the other specimen.

The patient was a man aged 34; and the disease was of six months' duration. There are two ulcers. The larger was nearly the size of a shilling, but irregularly square; situated quite centrally, and extending from the floor of the mouth almost to the tip of the tongue. The edge on one side was finely nodular, on the other slightly bevelled. The base was of a greyish-yellow colour and fairly smooth, and about $\frac{1}{8}$ to $\frac{1}{4}$ inch below the surface. The frenum was destroyed by the ulcer. Like the other case there was only slight induration of one edge, and no signs of new growth. Microscopically the tubercular tissue has not infiltrated so deeply into the tongue.

The smaller ulcer, situated at the side of the larger one is about the size of a threepenny piece, irregular in outline and shallow.

The submaxillary glands were only very slightly enlarged.

This patient also had phthisis. There were signs of consolidation and breaking down at one apex.

The front teeth were rather sharp inside, and the man had been in the habit of smoking an ordinary clay pipe, and I cannot help thinking that this was also probably a case of inoculation of an abrasion by bacillary sputum. *January 5th*, 1892.

3. *Large congenital cyst under the tongue.*

By Stephen Paget.

This cyst was removed from beneath the tongue of a little girl about four years old, a patient of Dr. Mitchell, of Brockley. She is the youngest of ten children; her mother suffers from cancer of the breast.

At birth, the child was almost suffocated; the cyst protruded in such volume from the mouth that delivery of the child was very difficult, and she was in great danger of suffocation. Dr. Mitchell at once tapped the cyst, and drew off nearly a tumblerful of clear watery fluid. The cyst was tapped twenty times or more during the first year of the child's life; further operation was declined till now.

The cyst (see fig. 4) hangs down out of the mouth, almost touching the sternum; it jerks up and down with movement of the tongue; the child can swallow fluids and soft solids, and can speak intelligibly. The cyst is covered with a harsh dry cuticle as thick as skin; the muscles of the tongue are spread out over its posterior and upper aspect; in front of its under aspect, the mucous membrane of the floor of the mouth is lifted up to a level with the lower teeth. The lips are tense and everted; the lower jaw is greatly deformed, flattened, twisted, and rotated outward and downward, so that the front teeth look forward and downward, and the back molars lock behind the corresponding teeth in the upper jaw.

I separated the cyst, between two curved incisions, from the tongue above it, and from the mucous membrane of the floor of the mouth beneath it, and removed it without difficulty, and united the edges of the tongue to the mucous membrane of the floor of the mouth. The child did well, and can now almost close her mouth; and the lower jaw is beginning to regain its shape.

The cyst contained some ounces of turbid yellowish fluid. It was well-defined, with a thick wall; there was no solid growth either inside it or around it. The wall was of simple fibrous tissue, lined with granulation tissue; there was no trace of epithelium in it.

The circumscribed, isolated nature of the cyst, and the absence

of any solid growth round it, exclude it from the category of "cystic hygromata"; and the character of the fluid drawn from it at birth, and the absence of an epithelial lining to it, seem to show

FIG. 4.

Large congenital cyst under the tongue of a little girl. The muscles of the tongue were thinned out and strained over it; the lower jaw was flattened, twisted, and rotated forward and downward. The child could swallow soft solids, and could speak fairly plain. The cyst was easily shelled out.

it was not a dermoid cyst. It may, as Mr. Sutton has suggested, have arisen in the thyroid duct; or it may have been a true serous cyst, similar to those congenital cysts in the neck which are described under the name of "hydrocele of the neck."

May 17*th*, 1892.

4. *A case of carcinoma of the œsophagus extending downwards along the rugæ in a patient who had been treated by continuous catheterisation.*

By W. B. HADDEN, M.D.

THE patient was a man, aged 38, who had had syphilis twenty years previously. He began to have difficulty in swallowing about six months before admission.

On admission he was unable to take solid food, and had much difficulty even in swallowing liquids. He referred the obstruction to the upper part of sternum. There were some old scars in the pharynx, but no other evidence of former syphilis in any part of the body.

Four days after admission an œsophageal bougie, the size of a No. 5 English catheter, was passed through the stricture, which was found to be situated nine and a half inches from the teeth. The tube was left in, and the patient was fed through it during the day. Three days later he was transferred to a surgical ward.

From April 7th to June 28th he was treated by catheterisation. The instrument was left *in situ* for three days at a time or longer, and then changed for a larger one when possible. At first a No. 6 catheter was passed, and subsequently the stricture admitted to No. 10. He was fed entirely by the tube for a period of about eight weeks. The stricture appeared to be dilating satisfactorily, so continuous catheterisation was stopped, and he was allowed to take nourishment by the mouth, a bougie being passed twice a week. Finally a No. 19 English catheter was introduced through the stricture.

He improved very much, and was able to swallow minced meat. He soon, however, began to go down hill; the dysphagia became very marked, and the size of the bougie had to be gradually diminished. At the end of eleven weeks from the commencement of treatment (June 28th) the obstruction was so great that only No. 5 could be passed with difficulty. The next day gastrostomy was performed.

From that time up to the date of his death, which occurred a

fortnight later, he was fed by nutrient suppositories and nutrient enemata alternately every four hours, and three times daily food was introduced into the stomach by a rubber tube.

At the *post-mortem* examination a mass of new growth was found infiltrating the walls of the œsophagus for a vertical extent of four inches, the upper limit of the growth reaching to a point two inches from the upper end of the œsophagus. Masses of growth projected into the gullet, so that it was possible to pass only a No. 8 catheter through the stricture. The growth was firmly adherent behind to the bodies of the vertebræ, and during removal a small perforation in the posterior wall was laid bare. In the lower half of the œsophagus the growth extended downwards from the main mass in uninterrupted lines nearly to the cardiac orifice, the lines clearly corresponding to the rugæ, and chiefly to the rugæ on the anterior wall. A small, slightly raised nodule of growth, the size of a split pea, was found on the mucous membrane of the stomach, just beyond the junction with the œsophagus. There were a few small secondary growths in the liver and spleen. A portion of growth from the œsophagus was examined microscopically, and proved to be squamous-celled epithelioma.

November 17*th*, 1891.

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5. *A large fibroma of the small omentum.* (*Card specimen.*)

By J. Jackson Clarke, M.B.

The patient was a woman, aged 50, and considerably emaciated. The tumour caused great prominence of the abdomen. There was a narrow band of resonance between the pubes and the growth, but above this there was continuous dulness, till at the level of the upper border of the fifth ribs in the mid-clavicular line the lung-resonance was reached. The growth was very hard and absolutely fixed. The patient had been aware of the presence of the growth for over four years. It had increased steadily in size, but during the last year it had occasioned so much pain that she was anxious to try any possible means of relief.

Mr. Owen having concluded that complete diagnosis was impos-

sible without exploration, and that the growth was probably a fibroma arising in the retro-peritoneal tissue and coming forwards above the stomach, made an exploratory incision. He found between the growth and the parietes, especially in the loins, firm vascular adhesions in such numbers that removal was impossible. The woman lived eight days after the exploration, and then she died of syncope. After death the wound and the peritoneum were found to be healthy. There were congestion and œdema of the lungs and ante-mortem clots in the heart, the muscular substance of which had undergone fatty degeneration.

The growth was situated between the layers of the small omentum, which could be separated from its outer surface by breaking down the very numerous vessels which passed into it from the sub-peritoneal plexus. Its upper extremity was adherent to the Spigelian lobe of the liver. There were no adhesions between the posterior surface of the growth and the peritoneum over the pancreas. The latter was flattened, and the retro-peritoneal tissues about it were indurated by chronic inflammation. The shape and position of the stomach and the duodenum were changed. There were several small blood-cysts in the tumour. There were small fibro-myomata in the uterus.

Remarks.—The tumour probably had its origin in the cellular tissue of the small omentum. While the growth was still small, and not fixed by adhesions, the diagnosis might have been made. Its mobility would have distinguished it from retro-peritoneal growths. If it lay over the aorta it might have simulated aneurism, but examination in the elbow-knee position would have distinguished it. I think the condition must be a very rare one.

February 2nd, 1892.

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6. *Dermoid cyst attached to the omentum.*

By Joseph Griffiths, M.D.

A large globular thin walled cyst, about 4½ inches in diameter, was found adherent to the lower part of the omentum, the connection looking like one of simple adhesion. The cyst wall

was very thin throughout and composed of fibrous connective-tissue, in which I could find no evidence of dermal structures. It contained a thick creamy fluid which, after removal from the body, soon solidified into a solid cake of substance like tallow, and in the interior was found a mass of entangled hair and two small spiculated lumps of dense bone.

It was removed from a woman, aged 35 years, who had borne children, and who detected it only six months prior to its removal by Sir George Humphry. Its connection is unusual, and, so far as I have searched, I can find no similar case, and the only instance I know that may give a clue to its real seat of origin is one referred to by Mr. Knowsley Thornton in a paper on "Peritoneal Cysts" in the 29th volume of the 'Transactions' of this Society, in which he says he had met with a multilocular cystic tumour in the omentum. I am inclined to regard this case as an example of dermoid cyst of the ovary becoming pedunculated, acquiring adhesions to the omentum, and ultimately having its original connection severed. It may be held that the cyst had its origin in the omentum, but from the manner in which the membrane has spread out upon the sac, that seems to me to be highly improbable. *February 2nd*, 1892.

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7. *Diphtheritic membrane in the stomach.* (*Card specimen.*)

By Edgar Willett.

The stomach of a child who died from diphtheria. Nearly the whole of the mucous surface is covered by the fine flaky "false membrane" of diphtheria. When fresh, the mucous membrane was red and acutely inflamed, and the "false membrane" of the usual ashen-grey tint. It had not spread beyond the pylorus.

From a child aged 1½ years; tracheotomy had been performed some time previously. At the *post-mortem* examination the pharynx was affected, but the œsophagus was normal.

See 'St. Bartholomew's Hospital *Medical Post-mortem Register*,' vol. xvii, p. 331, and No. 1918b in Museum. *April 5th*, 1892.

8. *Hypertrophy of the pylorus in an infant seven weeks old.*

By G. Newton Pitt, M.D.

The specimen consists of a stomach from an infant seven weeks old, who was under the care of Dr. Goodhart, to whom I am indebted for permission to publish the case.

The wall of the stomach is hypertrophied and rigid; its density is increased. At the inspection it was tough and fully distended, retaining its shape when the viscera lay on the table, although it was empty.

The pyloric portion for rather more than an inch forms a large fusiform tumour five twelfths of an inch thick, which consists entirely of hypertrophied muscle, as confirmed by microscopical examination.

The duodenum was empty and quite healthy; the entrance of the bile duct was patent and the lumen normal; there was no stenosis obvious.

The duodenum bent sharply on the hypertrophied pylorus; but it would hardly appear possible that this could give rise to any obstruction. The rest of the viscera were normal.

The history is briefly as follows:

The child was a healthy well-nourished baby until February 25th, 1891, when it was three weeks old. It was admitted for vomiting, and the colon was found distended with scybala. On March 1st it was discharged, relieved.

When readmitted on March 5th it had vomited continuously since the 1st, and its bowels had not been opened.

With treatment the bowels became more regular, but although carefully dieted with beef-juice, whey and cream, and later with peptonised milk, the vomiting was only partially prevented, and the child emaciated.

On March 18th the child became convulsed, collapsed, and vomited incessantly until its death.

I am entirely at a loss to offer any explanation of the hypertrophied condition of the pylorus. Undoubtedly there must have been some especial difficulty in the escape of food through the pylorus, and this led to the general hypertrophy; but it is

improbable that the unusually sharp flexure of the duodenum, which was noticed, could have been the origin of the trouble.

There certainly was no malformation leading to stenosis in connection with the hepatic duct.

Dr. Goodhart thought during life that the child possibly had some partial intestinal obstruction, and the symptoms, which failed to be relieved by treatment, would support the view that the abnormal condition of the stomach was the cause of death.

Landerer and R. Maier state that they have met with a similar condition. *October 20th*, 1891.

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9. *Destructive adenoma of stomach with thrombosis of right innominate vein.* (*Card specimen.*)

By F. C. Turner, M.D.

The specimens exhibited are:—1. A stomach laid open along its greater curvature, showing an extensive fungating growth extending over a great part of the posterior wall. In the smaller curvature it extends from about 2 inches from the pylorus to about 1 inch from the cardiac orifice. It has not encroached much on the anterior wall, but posteriorly it has extended to the greater curvature. The growth is soft and much degenerated, the edges only showing unchanged growth. There is an ulcer of the size of a florin in the centre of the growth by which the adherent pancreas has been exposed. Near the middle of the greater curvature there is a small perforation, which appeared to have been covered by adherent omentum, no extravasation of gastric contents having occurred. Nodules of growth appear on the peritoneal surface at the greater curvature, and the coronary vein there is seen distended and plugged by growth within it.

Sections of a nodule of secondary growth in the liver show the structure of a destructive adenoma, consisting of alveoli with a well-defined lining of columnar epithelium and with wide lumen filled with nucleated cells and detritus, separated by rather scanty fibro-nucleated stroma.

2. The heart and great vessels connected with it, from the same patient, showing incomplete occlusion of the termination of the right innominate vein by an adherent and apparently organised thrombus, and a pedunculated polypoid thrombus of the size of two large peas and of more recent origin, connected with the proximal extremity of the older thrombus, and hanging free in the vena cava.

3. A small piece of tissue showing the continuation of the right innominate vein, with parts of the right internal jugular and subclavian veins, and of the arterial trunks and cords of the brachial plexus in relation with them.

The internal jugular is completely filled with an organised thrombus, its walls are much thickened and its channel contracted. A smaller vein joining it near its termination is similarly thickened and plugged. The right subclavian is only partially obstructed by a conical thrombus adherent to its wall at its termination. The walls of this vessel appear normal.

The aorta is very atheromatous and the ascending portion dilated.

The specimens were obtained from the body of a man aged 44, a hawker, and previously in the Marines.

He was admitted into the London Hospital under my care on July 6th, 1891, with œdema of right arm and shoulder and side of the neck, and of the legs, which had been observed about two months. He was anæmic and had lost flesh, having been out of health since September, 1890, when he had, for the second time—a similar attack having occurred two years before—some hæmatemesis and melæna, losing a large quantity of blood. He then attended the Metropolitan Hospital for nine weeks as out-patient, and subsequently returned to work. Some three months later he attended a dispensary on account of shortness of breath and general weakness. Subsequently the swelling of his right arm and shoulder appeared, extending up to his right ear, and swelling of his legs was observed about the same time. Getting no better he came to the London Hospital.

He had at this time no gastric symptoms and took the ordinary diet. There was notable enlargement of the veins of right side of the chest and arm with œdema; the right arm measuring ¾ inch more than the left in circumference. There was also some œdema of the legs and ascites.

These symptoms disappeared under treatment by rest in bed, and iodide of potassium, suggested by a history of a "chancre" twenty years before, though unattended by any secondary symptoms, and in the absence of any recognised evidence of syphilitic disease; and the man left the hospital on August 7th and went to a convalescent home.

He admitted heavy spirit drinking while at sea, and rather free beer drinking since, and it was thought that the ascites and œdema of the legs might be accounted for by some cirrhotic condition of the liver.

Towards the end of August he began to suffer from epigastric pains and his abdomen began to swell, and subsequently the swelling again appeared in his legs. He was readmitted on September 28th.

For a week or two his appetite had failed, and he had been vomiting a good deal. He had lost flesh rapidly, and was much wasted and very weak. The abdomen was swelled, and painful when pressed or when he was moved. The legs were œdematous, but there was no swelling of either upper limb or of the neck, though the subcutaneous veins under the right clavicle were enlarged.

The man became gradually weaker and more emaciated, taking little food, though there was no sickness after October 1st, and died on October 13th.

The autopsy showed that there had been general adhesive peritonitis, by which the intestinal coils were matted together and adherent to stomach and liver and abdominal parietes, and more recent and acute peritonitis, attended with much turbid exudation, which filled the pelvis, and the formation of much curdy lymph in that situation and on the surface of the intestines. The spleen was enlarged, weighing 12 oz., firm and fleshy. The aorta was very atheromatous and its ascending portion dilated. The liver contained one nodule of secondary growth about 2 inches in diameter, with a large branch of the portal vein going to the centre of it, occupied by a cylindrical mass of growth rounded off at its proximal extremity. In the mesentery, contiguous to the ileo-cæcal valve, were some encysted collections of putty-like material. There was no ulceration of intestines. The transverse colon was adherent to the stomach but not invaded by the growth.

October 20th, 1891.

10. *Sarcoma of the duodenum.*

By H. D. Rolleston, M.D.

The mucous membrane of the first, second, and the commencement of the third, parts is greatly altered; the surface is raised and rough from plaques of material, which to the naked eye resemble hardened Peyerian patches. This growth is ulcerated and has broken down to some extent in the region of the biliary papilla, and again at the commencement of the third part the destruction of tissue is considerable. In the latter situation there is a cavernous ulcer passing up behind the pancreas, its walls, which are rough and irregular, are formed by the muscular coats infiltrated with new growth. There are several enlarged glands infiltrated apparently with new growth, adherent to the outer walls of this ulcer.

On the floor of this ulcer the inferior pancreatico-duodenal artery is exposed, and eroded in two places, of which one is firmly closed by new growth, while the other is freely open.

The pancreas is not itself infiltrated with new growth, but is expanded over the enlarged and infiltrated lymphatic glands. Neither the common bile-duct or Wirsung's duct were dilated. There were no gall-stones in the ducts or in the gall-bladder. The glands in the portal fissure were infiltrated. There were no growths in the liver. Pressure exerted on the gall-bladder did not induce any flow of bile out of the biliary papilla in the duodenum. The mucous coats of the stomach, the jejunum, ileum, and colon were quite normal. The glands in the mesentery were enlarged, and contained new growth similar to that in the glands around the pancreas. There was a large quantity of recently extravasated blood in the stomach and small intestine.

Microscopical examination.—Sections through the margin of the growth showed that the submucous coat was the part primarily affected. It is occupied by cells of somewhat varying sizes, but mostly either small or medium-sized round cells. The nuclei are relatively large to the scanty surrounding cell-substance; in form they are round, with a few exceptional oval ones.

In washed sections some delicate fibrils can be made out between

the cells. In addition there are coarser fibres, many of them probably derived from the tissues which the growth has invaded.

The growth passes from the submucosa upwards through the muscularis mucosæ between the crypts of Lieberkühn, the cells of which are proliferating. In the greater part of the duodenum the mucous coat is gone, and its place is taken by a mass of new growth in which blood-channels devoid of any proper walls are visible. The surface of the growth is ulcerated.

The growth projects downwards and infiltrates the muscular coats, passing between the muscular bundles and fibres and compressing them.

The growth is a sarcoma arising in the submucous coat of the duodenum, and has some resemblance microscopically to a lympho-sarcoma.

The infiltrated lymphatic glands showed microscopically a general obscuring of their structure, the normal arrangement being lost. The whole organ is crowded with cells of much the same type as those in the original growth in the duodenum.

The point of interest about this specimen is whether it is to be considered to be a sarcoma or that variety of sarcoma called a lympho-sarcoma. Its origin in the submucous coat suggest that it is a lympho-sarcoma, and the occurrence of some delicate fibrils between the cells may be considered to support this view. On the other hand, the cells are not small round, but medium-sized round cells, with some of various sizes, and the delicate fibrillar network is somewhat scanty. When lympho-sarcoma attacks the intestine it is generally widely distributed, and is most marked in the ileo-cæcal region, while the mesenteric glands are enlarged and infiltrated independently and not secondarily.

Dr. Norman Moore ('Trans. Path. Soc.,' vol. xxxiv) has recorded a case of lympho-sarcoma limited to the duodenum, but here the mesenteric glands were simultaneously occupied with growth.

In balancing the two alternatives it seems most probable that the growth is a sarcoma, and not a typical lympho-sarcoma.

The patient was a woman aged 30, who was in good health till Christmas, 1889, when she had influenza, from which she never properly recovered.

In August, 1890, she was obliged to give up work from progressive weakness, and from the frequent eructations of offensive gas

smelling like rotten eggs, which prevented other people from being in the same room with her.

At Christmas, 1890, she took to her bed. At this time gastric ulcer was diagnosed by a doctor.

In July, 1891, she was admitted to St. George's Hospital under the care of Dr. Whipham. She suffered great pain in the back, emaciated rapidly, and died with hæmatemesis in September, 1891.

January 5th, 1892.

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11. *Colon pigmented from mercury.* (*Card specimen.*)

By H. D. Rolleston, M.D.

The cæcum and colon are shown; they are uniformly pigmented. There was no pigmentation in the small intestine. There was no evidence of ulceration or inflammation in any part of alimentary canal.

Having in mind the case recorded by Dr. Theodore Williams in vol. xviii of the 'Pathological Transactions,' p. 111, of an old lady who for the last forty-three years of her life had been accustomed to take a grain of calomel every night, and whose colon was pigmented, I asked Dr. Rideal, Lecturer on Chemistry at St. George's Hospital, to examine the specimen. This he most obligingly did, and reported that "the tissue contains a mercury compound soluble in hydrochloric acid."

Microscopically, amorphous masses are seen to be situated in the mucous membrane, apparently in and between the cells of Lieberkühn's crypts; there are no pigment granules below the muscularis mucosæ. In Dr. Williams's case the pigment is described as being situated in the submucous tissue, viz. below the muscularis mucosæ.

The patient, a man aged 64, had syphilis when 44 years old. Whether he was treated for this I have not been able positively to make out. Eight months before his death from bronchitis he became an out-patient at St. George's Hospital for a sore of doubtful character on his tongue. He then underwent antisyphilitic treatment.

Since the colon contains mercury, and the mucous membrane

amorphous pigment, I have thought it probable that the pigmentation is due to the deposit of mercury in the mucous coat of the bowel. *November 3rd*, 1891.

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12. *An intestinal concretion, the surface of which was covered with large prismatic crystals of triple phosphate.*

By Hector W. G. Mackenzie, M.D.

A woman, aged 70, who had been a sufferer for many years from constipation, took a large dose of salts to relieve her bowels, which had not been opened for some days. When the bowels were moved, she was much alarmed at finding what felt like a hard bony mass presenting itself at the anal orifice. This, as afterwards turned out, was a concretion, but she imagined at the time that part of her body, perhaps her backbone, was coming away, and she made every effort to retain it in its position. She succeeded in pushing it back into the rectum where it remained for four months, at last coming away one day in spite of her.

At the time the concretion was voided, some of it broke off, so that originally it was larger than it now is. It is about the size of the astragulus and weighs 497 grains. It is irregularly cuboidal, and its surface is almost entirely covered with large crystalline prisms grouped in parallel columns. These crystals give to the concretion a most remarkable appearance, making it not unlike a miniature model of a mass of columnar basalt. One of its sides is irregularly concave where the fragments have been separated, and here projects a peg-shaped knob of bone or ivory.

Dr. Bernays has very kindly submitted the specimen to chemical examination, and has reported that the crystals consists of ammonio-magnesian phosphate with a trace of organic material. The nucleus burns like bone or ivory, and from its hardness he concludes that it is the latter.

The concretion was sent to me by Dr. J. A. Mackenzie, of Balham, under whose care the patient had placed herself. While the concretion was in the rectum Dr. Mackenzie made a digital examina-

tion, and feeling this hard irregular body quite high up, he not unnaturally concluded that the patient was suffering from malignant disease. The only explanation that the patient can give to account for the ivory nucleus of the concretion is that sixteen years previously one of her upper central incisors was broken and she swallowed the fragment. The stump is still in position in the jaw.

Intestinal concretions, other than gall-stones, in the human subject, if we except those which form in the vermiform appendix, are nowadays of extremely rare occurrence, at least in this country. Fifty years ago, to judge from the writings of that time, they were not so uncommon, and their occurrence was usually attributed to the large quantities of magnesia then consumed for medicinal purposes.

The concretion is of no remarkable size, being indeed quite small in comparison with some that have been recorded, as, for instance, by Mr. Jonathan Hutchinson in the sixth volume of the Society's 'Transactions.' Its appearance, however, is so remarkable that few who have seen it can credit that it has had its origin in the intestine. In vol. xxxvii of the Society's 'Transactions' Mr. Hurry Fenwick has recorded an intestinal concretion, in which crystals had been deposited on the surface; but the latter in his case was mammillated like a mulberry calculus instead of having the irregular columnar structure so striking in the concretion I have shown to-night. *November 17th*, 1891.

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13. *Two perforations in the vermiform appendix; peculiar enterolith.* (*Card specimen.*)

By H. D. Rolleston, M.D.

There are two perforations in the vermiform appendix. The first near the tip; a small fæcal concretion had ulcerated its way out, and set up a localised abscess. The second close to the cæcum; projecting through an ulcerated opening, was a sharp thorn, which was embedded in a hard calcareous mass the size of the last joint

of the little finger. This ulceration had set up a large retro-peritoneal abscess, which lay behind the cæcum, colon, and right kidney, and which had pointed and been opened in the groin; the abscess contained fæcal matter. There was no peritonitis.

From a woman, aged 55, who had no symptoms pointing to the cæcum until three weeks before death.

The points of interest are the age of the patient, the peculiar enterolith, and the presence of two ulcerated openings in the appendix. It is possible that the ulceration at the base of the appendix, round the thorn and calcareous mass, had predisposed the remainder of the appendix to become gangrenous by cutting off its blood supply. The proximal ulceration is on the concave border of the appendix, where the principal artery runs along the attachment of the mesentery.

March 15th, 1892.

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14. *Case of ulcerative colitis.* (*Card specimen.*)

By W. S. Lazarus-Barlow, M.B.

The patient, a young woman, was admitted to St. George's Hospital two months before death, having had some symptoms three weeks previous to admission. The condition was undiagnosed during lifetime. There were a few slight attacks of diarrhœa during her stay in hospital, but nothing which really could suggest that the intestine was the primary cause of the evil. Five days before admission she had shivering pains in the muscles, headache, and prostration, to which were added acute abdominal pain, vomiting and diarrhœa.

At the autopsy the abdomen contained free gas. There was old and recent peritonitis throughout the whole abdomen. In the pelvis was an old circumscribed abscess containing some fæcal matter. In the lower part of the descending colon were several transverse ulcerated openings on the anterior surface, from which fæces readily escaped; the gut above was slightly hypertrophied and very soft; the gut below was collapsed. In the transverse colon was an undermined ulcer not perforating the bowel. There was no other ulceration.

The case is of interest in that there was nothing to lead to a suspicion of the existence of the lesion in life, and in that it differs by the remarkable absence of general ulceration and the prominence of the perforation from the cases described by Dr. Hale White in the 'Guy's Hosp. Rep.' for 1888. Cases have been shown before this Society, and in particular I would refer to those by Dr. Ormerod ('Trans.,' vol. xl, p. 109), where there were both extensive ulceration and extensive perforation, and by Dr. Sharkey ('Trans.,' vol. xlviii), all of whose cases were accompanied by perforation. A very similar specimen is to be found in the museum of St. George's Hospital. *May 3rd*, 1892.

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15. *Ulceration of large intestine after fracture of the spine.* (*Card specimen.*)

By J. H. Targett, M.S.

This specimen (R. C. S. Museum, No. 2466 C.) is a portion of the large intestine of a man, aged 50, who died on the fifth day after fracture of the spine. The mucous membrane shows many superficial oval ulcers, varying from one eighth to half an inch in diameter. A dark slough, with partially separated edges, occupies the centre of several of these ulcers; but in other parts, where the slough has become detached, the submucous tissue, or even the muscular coat, forms the floor of the ulcer. The mucous membrane between the ulcers appears to be natural. Histologically, the submucosa at the seat of ulceration is much thickened and crowded with small round cells. At the edge of the ulcer the Lieberkühn's follicles are imperfect, and somewhat disarranged by infiltration of the intertubular tissue with small round cells. Where the central slough remains the floor of the ulcer is covered with an adherent granular pellicle, apparently structureless.

History.—The patient, a man aged 50, was pushing a truck, when an engine came up behind, struck him in the back with the buffer, and knocked him down, dragging him about thirty yards. He was admitted to a hospital two days later with complete paralysis of both legs, but no loss of sensation. Reflexes absent; no ankle-clonus; both sphincters paralysed. The same day (the

second after the accident) persistent diarrhœa set in, and continued up till the time of his death. The material passed was very watery, and was constantly running away. Death occurred from respiratory interference on the fifth day. The highest temperature, 103·4°, was reached the day before he died.

At the autopsy there was an oblique fracture of the lumbar spine, passing through the third and fourth vertebræ, the lower fragment being dislocated upwards and to the right. The spinal canal showed no extravasation of blood either outside or inside the dura mater; and there were no naked-eye signs of injury to the cauda equina nor to the spinal membranes. The stomach and small intestines were healthy, but the ulceration of the colon, of which the preparation exhibited is an illustration, was uniformly distributed throughout its whole length. It was particularly noted that the colon contained no scybala, in fact was practically empty. The kidneys showed early granular changes, and the liver was riddled with holes from the gases of decomposition, although the patient had only been dead about seven hours.

Dr. Acland has recorded in 'Trans. Path. Soc.,' vol. xxxvi, p. 56, two cases of ulceration of the intestines associated with paraplegia, and discussed the interesting question whether such ulceration may not be regarded as trophic in origin and comparable to an acute bedsore. In 'Guy's Hospital Reports,' vol. xlv, p. 157, Dr. Hale White mentions a case of descending lateral sclerosis in which four days before death severe diarrhœa set in, and the autopsy revealed intense colitis. But on this slender evidence the existence of a trophic form of intestinal ulceration cannot be established, though these four cases are very suggestive of such an occurrence.

May 3rd, 1892.

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16. *Polypus of small intestine associated with intussusception.*

By C. B. Lockwood.

The polypus was globular, and had a diameter of about three quarters of an inch. It was fastened to the wall of the ileum by a short neck. Its point of attachment was about 2½ feet

from the cæcum. It was of a firm consistence, and covered with mucous membrane, with its interior composed of fibrous and muscular tissue, and with a calcareous nodule in the centre. Below the polypus was an intussusception about 5 inches long. The mesentery having been dragged into the bowel with the intussuscepted gut the tumour was held against the posterior abdominal wall. As these conditions caused intestinal obstruction, laparotomy was done, but all attempts at reduction were unavailing, and therefore the intussusception was excised. Owing to collapse, the ends of the ileum were not united, but brought out of the wound by Mr. Thomas Smith. The polypus was discovered during this operation and was removed. It seemed clear that the polypus was of long standing. The patient was a woman aged 30. The calcareous nodule suggested that it had been present for many years. The occurrence at or near the position of the vitelline duct suggested that it had a congenital origin. It was probable that the sequence of events was that the polypus had caused an obstruction, and the intussusception had been formed during violent peristalsis, and the lower gut had invaginated over the upper. *May 3rd*, 1892.

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17. *Ileo-colic intussusception caused by an inverted Meckel's diverticulum.*

By James Adams, M.D.

W. C—, aged 42, labourer, hitherto in good health, was attacked on April 27th, 1891, with symptoms of intestinal obstruction. Under treatment he recovered and in a week was able to resume work. On May 18th the symptoms returned, but were not relieved by treatment. The vomiting was only slight, and during the last week of his life it ceased altogether. A small quantity of blood was passed *per anum* on one occasion after an enema. The temperature never exceeded 99·8° and was subnormal several times during his last illness. There was some fulness with dulness over right iliac region, but no tumour could be made out. He died on June 9th with peritonitis and intestinal obstruction.

On making a *post-mortem* I obtained the accompaning specimen, which consists of lower portion of ileum, cæcum with vermiform appendix, and ascending colon, and shows an ileo-colic intussusception. The ileum, where it passes with the mesentery through the ileo-cæcal valve, is constricted, black in colour, and evidently on the point of becoming gangrenous. A bristle is passed through the ileum and comes out in the ascending colon at the further end of the entering layer. The ascending colon has been opened by a longitudinal incision, through which is seen the intussusceptum with mesentery. The intussusceptum has sloughed at its distal extremity, and the two layers and the mesentery were all firmly bound together by inflammatory adhesions, some of which I have separated. I made a longitudinal division of the last inch of the entering layer in order to fully examine a slender pyriform body which was lying in the lumen of this layer. It proved to be an inverted Meckel's diverticulum. It is situated 8 inches from the ileo-cæcal valve, is 3 inches in length, and is covered with mucous membrane. On making a small opening into it I found its interior filled by adipose tissue, which was loosely adherent to its smooth lining. By separating the adhesions which matted together the peritoneal surface and the mesentery, I found the opening of this inverted diverticulum was occupied by adipose tissue, and, on traction being made on what was filling its interior, it became evident that the contents were a piece of mesentery which had entered the diverticulum and had become adherent by an inflammatory process.

There are only two other specimens of inverted diverticuli associated with cases of intussusception that I have been able to find in the London museums. One is in Guy's Hospital Museum, referred to by Mr. Treves in his work on 'Intestinal Obstruction;' the other is in the Museum of St. Bartholomew's Hospital. These three specimens were all from males of adult life.

How this singular condition can arise it is not easy to determine. Possibly it begins by a dimpling of the free end of the diverticulum; this increases, forming an intussusception of the little tube, and, finally, it becomes completely inverted and hangs loose in the lumen of the ileum. It can then act as a polypus in producing an intussusception. *April 5th*, 1892.

18. *Two cases of hernia, complicated by tubercular implication of sac or contents.*

By Bernard Pitts.

The specimen shown was taken from a boy, aged 5, who was admitted into St. Thomas's Hospital on April 21st, 1891, with a rather large right inguinal hernia. The hernia was a reducible one, but had increased considerably in size during the year, and was constantly coming down, even with a truss carefully applied.

A radical cure was therefore recommended, the boy then being in apparently good health, and with a good family history. I operated on April 24th, and on opening the sac found the hernia was of the congenital form; the testicle was enlarged and had several tubercular nodules on its surface, and several nodules were seen on the lower part of the sac. The testicle and sac were therefore removed, and the abdominal opening closed in the usual manner. A little fluid was allowed to drain from the abdominal cavity before the neck of the sac was ligatured. Examination of the abdomen under the anæsthetic revealed the fact that several hard nodules could be felt above and to the left of the umbilicus, but there was no distension of abdomen or evidence of fluid to be made out by this examination.

The operation was followed by considerable rise of temperature and signs of general peritonitis; the wound, however, healed without suppuration, and the boy left the hospital convalescent on June 7th. He is now in good health—much stouter and stronger than he was before operation—and has been attending school for several months.

A section has been made through the testicle and epididymis. The nodules on the visceral layer of tunica vaginalis and on the lower part of the sac are well marked. At one place on the testicle these nodules have become confluent, and an appearance very like a hernia of testis is presented.

The cord and epididymis are normal, and the latter has been indicated in the specimen by blue glass placed between it and what represents the testicle.

Examination microscopically of a complete section, kindly made for me by Mr. Shattock, shows that in front of the normal epididymis is a mass of granulation tissue full of tubercular foci, and the tunica albuginea, much thickened, separates this from an aggregation of tubercular nodules, which to the naked eye seemed to represent a hernia testis.

When I first asked permission to bring the case before the Society, it seemed probable that the testicle was the primary seat of tubercular disease, and had infected the sac and the abdominal contents; but after the microscopical examination it would appear more probable that the testicle was first invaded from the surface, and this was secondary to some tubercular disease within the abdomen, and this view is thus more probable from the fact that the epididymis is not involved by the disease.

Cases, however, of tubercular disease of hernial sac or contents are sufficiently rare to serve as an excuse for bringing the case under notice, and it is quite conceivable that a tubercular process in the testicle might, by implication of a hernial sac, infect the peritoneal cavity of the abdomen, especially when the hernia is of the congenital form.

A very brief reference may be permitted to another case of tubercular hernia, in which there can be no question that the disease extended from the abdomen to the hernia.

J. S—, a lad aged 18, was admitted on December 19th, 1889, to St. Thomas's Hospital with a large irreducible inguinal hernia on the left side, and a small irreducible inguinal hernia on the right. His abdomen was swollen and tender, the hernial swellings were very painful, and the lad had been sick for several days with complete obstruction of the bowels.

At the time of his admission no proper history could be obtained, and the lad was too ill to answer questions as to previous history, but had been at work up to the onset of the vomiting and abdominal pain.

On making an exploration of the left hernia I found a mass of adherent tubercular omentum, which was commencing to break down. This was removed, and some sero-purulent fluid evacuated from the abdomen.

An incision over the hernia on the right side revealed a similar condition, and a median abdominal section was then made, but the

intestines were so matted by tubercular disease that it was only possible to wash out the abdomen to a very limited extent. The wounds healed readily, and the abdominal symptoms were considerably relieved.

He was afterwards transferred to the medical wards under the care of Dr. Payne, and died three months later from general tubercular mischief involving the heart, spleen, and intestines.

There was a history of phthisis on the mother's side, and of fourteen children six had died from tubercular disease of the intestines. *October 20th*, 1891.

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19. *Deficiency of the left half of the diaphragm; displacement of stomach and intestines into the thorax.* (*Card specimen.*)

By G. Newton Pitt, M.D.

The specimen consists of the trunk of a new-born fœtus, which only gave a few gasps after its birth and died. The left half of the diaphragm, with the exception of a ring of muscle round the margin, is deficient. Through this aperture the stomach, pancreas, and the intestines, with the exception of the colon beyond about the hepatic flexure, have passed into the thorax, the greater portion of which they occupy. The heart is displaced to the right, the left lung is compressed into a small mass ¾ inch long, and the right lung, which is reduced to one third its proper volume, is 1½ inches long. The liver is very large and occupies the greater portion of the space below the diaphragm. The infant presents no other obvious abnormalities.

This abnormality is very rare, and is incompatible with life.

Directly after delivering the child, Dr. Wills, of the Old Kent Road, noticed that the heart was beating on the right side of the chest, and forwarded the specimen to me, expecting that the abnormality would be a transposition of viscera.

May 17th, 1892.

20. *Rupture of liver; the rent closed by adherent blood-clot; death on the fourth day from peritonitis.*

By Edgar Willett.

This case was that of a lad, aged 15, under the care of Mr. Thomas Smith, who kindly gave permission for its publication. The lad, while riding a bicycle, was run into and struck on the right side, just below the ribs, by the shaft of a runaway cab. On his admission into St. Bartholomew's Hospital he was a good deal collapsed and vomited, his breathing being then abdominal. The next day tympanitis occurred; peritonitis set in on the second day, and he died in the afternoon of the fourth day. Rupture of the liver was diagnosed, severe injury to the intestine having been excluded from the comparative absence of symptoms for twenty-four hours.

At the autopsy the peritoneum was found distended and contained a large quantity of blood and bile-stained fluid; there was no pus or lymph or any foul smelling fluid; the small intestine was distended from the acute peritonitis which seems to have been largely started by the bile. The liver, now shown, was found to have an extensive tear four inches in length, but the edges were quite close together and adherent by means of a recent clot. There was no fracture of any ribs nor was the skin broken. The gall-bladder was intact.

The specimen is of interest, especially in connection with a rupture of the spleen exhibited by me last winter, when a tear had been united in a similar way, the patient in that case living forty-eight hours, and dying from other injuries. The specimen is now in the Museum of St. Bartholomew's Hospital, Series xxi, No. 2240[a].

October 20th, 1891.

21. *Nodular cirrhosis with hæmorrhages.*

By H. D. Rolleston, M.D.

The liver weighed 72 oz., its surface was irregular from the projection of yellowish white nodules of various sizes, the largest being as big as a nut. These nodules were not umbilicated, and resembled secondary new growths. On section these nodules stood up in marked contrast to the surrounding liver substance, which was deeply congested.

The portal vein was normal. The bile-ducts were pervious.

Microscopical examination.—The yellowish white nodules were composed of healthy liver-cells, in which no signs of fatty infiltration or degeneration could be made out.

The lobular arrangement is accentuated; at the margins of the lobule the liver-cells become compressed and flattened, so as to give the appearance of encapsulation. These flattened cells pass by gradations into the tissue forming the congested background seen by the naked eye.

In a few cases recent extravasation of blood has taken place into these collections of liver-cells; the blood is not in the region of the intralobular vein, but on the periphery, viz. near the flattened cells. The intralobular veins are normal, and show no signs of chronic congestion.

To pass on to the consideration of the greater part of the liver, viz. the areas which appeared deeply congested to the naked eye.

The most prominent feature was the frequent occurrence of recent extravasations of blood. In the blood thus poured out large nuclei are visible at intervals, which, in sections washed so as to remove the blood-corpuscles, were seen to belong to altered liver-cells. They are flattened out, so that, in profile, they have some resemblance to connective-tissue corpuscles. That they are not developing fibrous tissue elements seems clear from the facts, (1) that there is not any distinct small cell infiltration, and (2) that all stages of transition from healthy liver-cells to these anomalous cells can be traced. Part of the change in form is due to the pressure exerted by the extravasated blood.

In addition these cells are degenerating, and in places undergoing disintegration.

In the areas where hæmorrhage has not taken place the liver cells are in very various conditions; some are fairly healthy, some compressed, atrophied, degenerating, and breaking down. Among them are large nuclei derived probably from disintegrating liver-cells. It appears that no small cell infiltration is present.

Between and in some of these cells granules of golden pigment may be seen. Sections treated with ferrocyanide of potassium and with hydrochloric acid do not show more than a normal amount of free iron. From this observation it seems probable that the blood extravasation is of recent date. There are no casts of bile in the ducts or bile capillaries.

In places the changes in the liver-cells and hæmorrhages can be seen advancing into the healthy areas described above. Between the liver-cells there are thin-walled vessels distended with blood, which explain the extravasations elsewhere. There appears to be an increase in the portal areas of the normal fibrous tissue; it is not improbable that the degenerative changes in the parenchyma of the liver make Glisson's capsule more prominent. In any case, if there be an increase, it is of old standing and slight in amount.

The capsule shows hardly any thickening; under it the liver-cells are for some little distance separated from each other by an exudation product, which does not take ordinary stains well.

To sum up the microscopical appearances. There is a diffuse change in the liver-cells resulting in degeneration and going on to disintegration; associated with this are recent extravasations of blood.

The explanation of these phenomena is probably a subacute parenchymatous hepatitis, which by weakening the support of the small vessels has been followed by extravasation of their contents.

The degenerative changes in the liver-cells resemble those of acute yellow atrophy, though less extensive and not so advanced.

In Cornil and Ranvier's 'Manuel d'Histologie Pathologique,' vol. ii, p. 388, the condition of "hépatite parenchymateuse nodulaire" is described.

The appearances in my case are the same in kind but more

acute, and in addition accompanied by hæmorrhages, so that this case may be regarded as lying between acute yellow atrophy and "hépatite parenchymateuse nodulaire." The latter disease is ascribed by Kelsch and Kiener (quoted by Cornil and Ranvier, loc. cit.) to malarial poison; no such cause is forthcoming in the present instance.

The patient from whom this liver was removed was thirty-nine years old; he was of temperate habits, and had enjoyed good health till March, 1891, when for three weeks he had pains in the loins. This left him weak, and in the middle of July ascites developed. In September he was admitted into St. George's Hospital under the care of Dr. Ewart. His abdomen was twice tapped for relief of ascites. He was slightly jaundiced, and pigmentation of the nipples suggested the possibility of Addison's disease. Excavation of the apex of the left lung, fœtid expectoration, and occasional hæmoptysis came on, and death occurred on November 13th, 1891. The history does not record any acute disease or the occurrence of hæmatemesis. At the *post-mortem* there was no general acute or chronic peritonitis. The spleen weighed 13 oz. and was soft. The pancreas, suprarenals, and kidneys were normal.

The veins round the lower end of the œsophagus, those around the rectum, and the sub-peritoneal plexus of veins were dilated. The mucous coat of the intestines was very œdematous. The heart, 13 oz., was normal. There was a sloughing vomica at the apex of the left lung. *December 1st*, 1891.

Report of the Morbid Growths Committee on Dr. Rolleston's specimen of nodular cirrhosis.—The naked-eye appearance of the liver is certainly remarkable, the round, yellowish islands contrasting strongly with the deep red liver tissue around, and suggesting at first sight the presence of a new growth. Under the microscope the yellow islands appear to be made up of well-defined liver-cells. On the periphery of some of them are liver-cells which are elongated, flattened, and atrophied. A growth of somewhat abundant but delicately formed spongy connective tissue is developed irregularly through the organ. Broad strands of it are visible here and there, and in them we can see the liver-cells in various stages of flattening and atrophy. There is in addition an unusually large amount of extravasation of blood to be seen.

The disease evidently belongs to the class, cirrhosis of liver,

but the large yellow nodules, and abundant extravasation of blood, produce naked eye appearances which are uncommon.

A similar specimen was recorded by Dr. Goodhart in the thirty-sixth volume (p. 234) of the Society's 'Transactions.'

SEYMOUR J. SHARKEY.
FREDERIC S. EVE.
NORMAN MOORE, *Chairman.*

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22. *Syphilitic disease of the liver with gummata and extreme pericellular cirrhosis.*

By HECTOR W. G. MACKENZIE, M.D.

H. V—, a boy aged 15, was admitted under my care at the Royal Free Hospital on March 24th, 1891. He came complaining of cough and shortness of breath, but on examination I found he was deeply jaundiced and that the liver was much enlarged. His history shortly was that while he had had no definite illnesses, he had never been very strong, and had always been short of breath and liable to palpitation of the heart and bronchitis. Eighteen months before I saw him his father had died, and he had endured considerable privation since then. He had noticed the swelling in the situation of the liver for nine months, and since he first noticed it, it had increased in size. He had had slight tenderness over the liver, and it had pained him to lie on that side. For six months he had felt weak and had had a troublesome cough. He had rather rapidly lost flesh, and the weakness had increased during the past three months. The jaundice had only been noticed during the last fourteen days.

He was a small, ill-developed, badly nourished boy. The skin every where was yellow and dry, and the conjunctivæ were markedly jaundiced. There was no œdema. There was no evidence of constitutional syphilis either in the teeth, eyes, or conformation of the head.

The abdomen was distended, and crossed in every direction with dilated superficial veins. There was no detectable ascites. The

liver, as has been said, was enlarged, reaching in the nipple line nearly two inches below the umbilicus, and it felt irregular and nodulated. It was tender to palpation.

In addition to jaundice and irregular enlargement of the liver, another marked feature of the case was a thickening of all the superficial arteries. The radial, the transverse cervical, and the facial arteries felt like pieces of whipcord, and could be rolled under the finger.

There was very marked pulsation in all the visible arteries. A systolic murmur was to be heard over most of the cardiac area, but loudest over the pulmonary valve. A soft occasional diastolic murmur was to be heard to the right of the sternum.

There were no abnormal signs in the lungs. The urine was free from albumen, but contained abundant bile.

My first idea was that the case was one of malignant disease, but that would involve an independent explanation of the arterial sclerosis. It was an obvious suggestion that the case was of syphilitic origin, and I thought that syphilis might explain both the liver disease and the arterial condition. I was a little puzzled to account for the cardiac murmurs, but the systolic I believed to be hæmic on account of its situation.

As I have said, I could find no confirmatory evidence of syphilis, although I examined most carefully. The family history, I may add, threw no light on the case.

However, everything considered, I thought syphilis was most probably the cause of the disease, and accordingly, on March 28th, treatment with iodide of potassium was commenced, the boy being ordered five grains three times a day.

The iodide of potassium was continued for nearly four weeks. The boy felt better while taking it, but no change was perceptible either in the intensity of the jaundice or in the size of the liver. He was weighed on the 7th and 18th of April, and on the two occasions he weighed the same, although he had the appearance of being fatter than when he first commenced the treatment. A trace of albumen having appeared in the urine, and as he had some abdominal pain, I discontinued the iodide of potassium on April 23rd. On April 29th he was weighed, and was found to have lost 5½ lbs.

On May 6th he was put back on iodide of potassium at his own request, as he said it suited him best of all the medicines he had

tried. On the 1st of June the iodide of potassium was again discontinued, as he had developed a papular eruption, which it was thought might be an iodide rash, but he seemed to miss the medicine and he was, therefore, again put back on it on June 9th. He, however, gradually became weaker. The heart began to fail, dropsy and ascites developed, and the quantity of albumen in the urine increased. He died on July 6th.

At the *post-mortem* examination the heart was found to be organically affected. The aortic valve had only two curtains, a large and a small one, and these curtains were thickened; the left ventricle was slightly hypertrophied. The murmurs heard during life were thus satisfactorily explained. The liver was much and uniformly enlarged. There were two deeply depressed scars on the surface, one round the notch for the gall-bladder, the other on the upper surface firmly adherent to the diaphragm. The gall-bladder was much distended, and lay in a transverse direction towards the middle line below the edge of the liver. Its duct was imbedded in fibrous tissue, which had so constricted it that no fluid could pass from the gall-bladder into the common bile-duct. As usual in such cases, the gall-bladder contained quite colourless fluid. The common bile-duct was much dilated, as were also its branches, which, as well as the duct itself, contained green inspissated bile. On section the liver presented a very striking appearance. Quite two thirds of the sectional surface was mapped out into areas of olive-green or orange, surrounded by a ground work of deep claret colour, and intersected in all directions by strands of connective tissue. The cicatrix near the gall-bladder was of almost bony consistence, the fibrous tissue having undergone calcification. While there was no doubt that the deep scars on the surface were retrocedent gummata, the general appearance of the section very strongly suggested the presence of malignant disease. Microscopical sections taken from different portions of the field all showed practically the same change, an enormous overgrowth of connective tissue. This not only passed, as could be seen with the naked eye, round the groups of lobules, but was abundantly present in the lobules themselves, passing between individual cells or surrounding small groups of cells. Very few blood-vessels could be seen in this interstitial growth. In some parts, as the result of the compression to which they had been exposed, the liver-cells were atrophied and had under-

gone fatty degeneration, while in others the lobules appeared to have a cavernous structure, probably in consequence of the dilatation of the capillary bile-ducts. The condition was what has been previously described as the pericellular cirrhosis of syphilis.

Such a condition has been brought before the Society on several occasions, especially by Dr. Penrose and Mr. Charters Symonds, but this case differs from those previously recorded in two important respects:

First, all the other cases recorded in the Society's 'Transactions' have been from infants of a few weeks old, while the present specimen was from a boy fifteen years old.

Secondly, the combination of gummata with this form of cirrhosis has not been recorded before, and gummata in the liver are of not very frequent occurrence in the congenital form of syphilis, as this in all probability was.

It is worth while remembering the possibility of this co-existence of gummata with cirrhosis in connection with the treatment. Iodide of potassium could not be expected to do much in the disseminated form of syphilitic disease of the liver. The only benefit which seemed to result from the administration of iodide of potassium was that the boy felt better and improved in appetite.

There was no ostensible cause for the general thickening of the arteries, unless it were syphilitic. There was no sign of kidney disease. But general arterial thickening is not a recognised result of syphilis. *October 20th*, 1891.

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23. *Gall-stones encysted in a sacculus of the gall-bladder.* (*Card specimen.*)

By H. D. Rolleston, M.D.

The lower half of the gall-bladder is constricted off, and only communicates with the remainder by a narrow orifice admitting a bristle. This sacculus contains two rough calculi, one above the other, separated by a constriction of the walls of the

sacculus, which are very tightly drawn over them. There was no ulceration of the walls. The remainder of the gall-bladder contained bile and a few loose calculi, which were slightly facetted.

From a man, aged 55 years, who died in St. George's Hospital with gangrene of the foot. The gall-bladder has been cut open and incisions made over the encysted gall-stones.

December 1*st*, 1891.

IV. DISEASES, ETC., OF THE GENITO-URINARY ORGANS.

1. *Cystic adenoma of kidney.*

By Walter Edmunds, M.D.

[With Plate III.]

The kidney was removed during life from the body of a girl aged 18 years.

A moveable lump in the left lumbar region had been noticed about two years, during which time it had appeared to grow. The tumour was thought to be the left kidney, and so on operation it proved to be; the patient did well.

On examining the kidney after removal there was found, projecting from its anterior surface, a globular tumour; on section this was seen to be about 2½ inches in diameter and to project internally into one of the calices; except here the tumour is covered everywhere by a thin layer of kidney substance.

The tumour (which was enclosed in a separate capsule closely adherent to the substance of the kidney) was found to consist entirely of cysts; these were of various sizes, the largest being about 1 inch in diameter. The cysts contained a thin, colourless fluid, and on microscopic examination were found to be lined with an epithelium, in some places columnar, in some cubical. The remainder of the kidney was healthy, and was no doubt working at the time of removal.

I have been unable to find either in the 'Transactions' of the Society or elsewhere any record of a similar case.

Reasons have been given by Mr. Shattock, in a paper read before this Society (see 'Transactions,' vol. xxxvii, 1886), for thinking

that in some cases of cystic disease of kidney the affection is due to the growth of included remains of the Wolffian body; the fact that the tumour is in a distinct capsule seems to favour that view in the present case.

The accompanying drawing shows the appearance of this specimen after preservation in alcohol (see Plate III).

I am indebted to Mr. Croft, under whose care the patient was, for permission to exhibit the specimen. It is preserved in the Museum of St. Thomas's Hospital. *April 5th*, 1892.

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2. *Hydronephrotic atrophy of part of one kidney.* (*Card specimen.*)

By F. C. Turner, M.D.

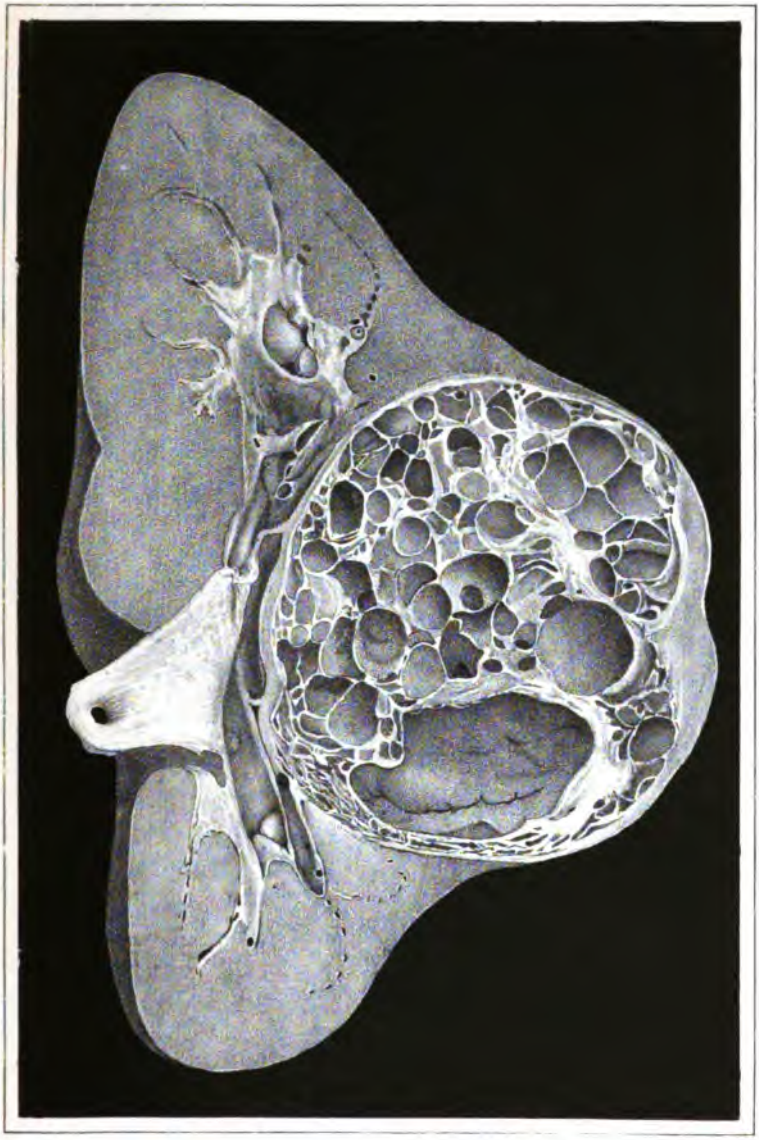
The specimen shows almost complete hydronephrotic atrophy, with some shrinking, of the lower two thirds of the right kidney. The upper end of the organ appears to be healthy. No communication could be found between the ureter and the part of the renal pelvis connected with the hydronephrotic part of the kidney. The left kidney was large, the two organs weighing together 10 oz. The heart was much hypertrophied and dilated on both sides, weighing 18 oz. No valvular lesion. There was recent pericarditis with abundant effusion, from which the patient appeared to have ultimately died. There was also an infarct at the base of the right lung, and three abscesses in the same lung. There was atheroma of the aorta, and the branches of the renal arteries were thick.

The patient was a woman, aged 38, who was admitted into the London Hospital with dilated heart and pericarditis. She had anasarca and ascites, and the urine contained about one eighth albumen. *January 19th*, 1892.

DESCRIPTION OF PLATE III.

Illustrating Mr. Walter Edmunds's specimen of Cystic Adenoma of the Kidney. (Page 89.)

The kidney has been divided vertically in an antero-posterior plane. The tumour, which consists of a congeries of cysts, is distinctly circumscribed, and projects from the posterior aspect of the kidney. Anteriorly its most prominent part projects into the renal pelvis.



F Huth, Lith^r Edin^r

3. *Tubercular growth in the ureter.*

By Nestor Tirard, M.D.

The specimens shown possess some interest, not only on account of the clearness of the renal changes consecutive to an obstruction in the ureter, but also on account of the relatively rare nature of this obstruction.

The specimens are from a boy, aged 5 years, who was admitted under my care at the Evelina Hospital for Sick Children, with general dropsy. There was a family history of tubercle, the mother having died of consumption and one brother of "inflammation of the brain." Although described as always delicate, the only definite illness seemed to have been measles. The dropsy commenced on October 2nd, but it was stated that during the previous week the urine had been of a bright red colour, offensive and scanty.

On admission there was some œdema of the face, aud the legs were swollen, and pitted on pressure. No albumen was found in the urine, which was of a light colour, sp. gr. 1015.

The œdema speedily passed off, but the child steadily grew worse, and harsh respiratory sounds, frequent diarrhœa, and wide oscillations of temperature, speedily led to a diagnosis of general tuberculosis. The child eventually died on October 19th, a fortnight after admission. The urine had been repeatedly tested, but was always found faintly acid and free from albumen. The specific gravity varied from 1010 to 1020.

Upon examination both lungs were found to be somewhat adherent to the chest wall; and adhesions, which were readily broken down, united the adjacent lobes. Over the roots of both lungs the pleural folds were studded with miliary tubercles, and the bronchial glands were large and caseous in appearance. Both lungs were infiltrated with tubercular nodules, some as large as a pea.

The peritoneum was thickly covered with tubercles, and the different coils of the intestine were firmly adherent. Tubercles were also found on the surface of the liver and spleen, and within the substance of the latter.

The left kidney was large, the pelvis much dilated, and a considerable quantity of urine escaped on removal. On section the

medulla was found to be thinned down somewhat and very pale. The apices of the pyramids were much atrophied, the calices widely dilated.

In the left ureter a hard nodule existed at about the junction of the upper and middle third of the tube, which was dilated above this point and constricted below. A probe could not be passed through this nodule without force. On slitting it open the ureter was found to be studded with small tubercles, and, at the nodular swelling, to be completely surrounded by a rugged mass, the surface of which was hard and rough, apparently from the deposition of salts (urates) upon a caseous surface.

The right kidney was relatively large and firm; the capsule stripped off easily; on section it showed deep congestion. The right ureter appeared normal.

Upon microscopical examination of the left kidney the usual appearances of consecutive cirrhosis were found; the epithelium in the tubes near the glomeruli was swollen and granular, that in the straight tubules somewhat atrophied, while the tubules were dilated irregularly. A relatively large number of nuclei was found over the Malpighian tufts.

With regard to the tubercular growth in the ureter, it is interesting to note that no tubercles were to be seen on the mucous surface of the bladder, or on the surface, or in the substance, of the kidney. *November* 17*th*, 1891.

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4. *Sarcoma of the ureter.* (*Card specimen.*)

By J. H. Targett, M.S.

The specimen exhibited was taken from the body of a man, aged 46, who was admitted to a hospital for hæmaturia and wasting. His illness began four months previously with severe pains in the loins and thighs, and at the same date he noticed for the first time blood and gravel in his urine. On admission a large tumour was found occupying the umbilical and right lumbar regions of the abdominal cavity, and the urine contained round

and spindle-shaped cells and blood-clots. The tumour rapidly enlarged, the emaciation became extreme, and the patient died five weeks after admission.

Autopsy.—The tumour was situated on the posterior wall of the abdomen, behind the duodenum and pancreas. It extended laterally from the right kidney to the left side of the lumbar spine, and in the vertical direction from the diaphragm to the brim of the pelvis. The aorta and vena cava were entirely surrounded by growth, and the latter was filled with thrombus from the level of the right renal vein to the middle of the common iliac veins. The pelvis of the right kidney was partially embedded in growth, and its cavity, together with the calices of the kidney, was widely dilated in consequence of the obstruction of the ureter. From its upper extremity to the bifurcation of the right common iliac artery the right ureter was surrounded and invaded by the new formation; below that level it passed to the back of the bladder as a large solid cord, in size and appearance on section closely resembling the spinal cord. Within the bladder the growth projected at the orifice of the right ureter as a polypoid tumour the size of a cherry, the pedicle of which was covered with healthy mucous membrane, but its summit around the opening of the ureter was superficially ulcerated. The liver contained numerous secondary deposits.

Histologically the tumour was a round-celled sarcoma. The invaded ureter was examined near its vesical end, and the microscopic sections showed that the lumen of the duct was entirely filled with small round cells and granular *débris*. The mucous membrane had disappeared, and groups of round cells were to be seen between the planes of the muscular coat.

The preparation is of interest inasmuch as the whole length of the ureter was invaded by a new growth from without, which having reached the interior of the duct filled and even distended its channel, and thus spread downwards to the bladder. In a somewhat similar case recorded in the 'Transactions' of this Society (vol. xviii, p. 159), the ureter was filled with malignant growth, apparently sarcoma, which had extended upwards from a primary source in the bladder. *December 15th*, 1891.

5. *A case of psorospermial cysts of the left kidney and ureter, and of the bladder, with hydronephrosis of the left kidney.*

By J. Jackson Clarke.

[With Plate IV.]

The literature of psorospermosis in general has been so fully collected by Professor Delépine ('Path. Soc. Trans.,' 1890, p. 366) that I need only recall some published cases of psorosperms affecting the kidney and urinary tract of mammals.

Rud. Virchow ('Archiv. f. Pathol. Anat. in Physiol.,' 1860, p. 527) mentions a case he had observed, thirteen years before that date, of psorosperms of the kidneys of a bat. The account is accompanied by a plate. The structures were "Offenbar Psorospermien."

Lindemann, in 1863 (quoted, with figure, in the English translation of Leuckart's 'Parasites of Man,' by W. E. Hoyle, p. 226), recorded the case of a woman who died of Bright's disease. "The parasites appeared as small naked masses. The organ was infiltrated with a mucous exudation which contained the well-known mucous balls of Hassall."

J. Bland Sutton ('Fowler's Dictionary of Medicine,' article "Psorospermosis") gives the result of the histological examination of a specimen of cystic ureter in the museum of the Middlesex Hospital. Psorosperms were found in the cysts. Mr. Sutton also refers to a specimen shown to the Pathological Society by Mr. Targett ('Trans.,' vol. xli, p. 170).

F. S. Eve ('Path. Soc. Trans.,' vol. xl, p. 444) reports, with a very remarkable clinical history, a case of psorospermial cysts beneath the capsule of the kidney.

W. B. Hadden ('Path. Soc. Trans.,' vol. xxxiv, p. 237) records a case of "multiple sarcoma." The Morbid Growths Committee of the Society submitted some of the kidney lesions to T. S. Cobbold, who gave the opinion that they were due to psorosperms.

The present specimen comprises the kidneys, ureters, and

bladder, removed from the body of a woman aged about sixty. She was admitted into St. Mary's Hospital, under Dr. Lees, in a dying state. After death a large hæmorrhage into the right cerebral hemisphere was found. The arteries at the base of the brain were extremely atheromatous. There was hypertrophy of the left ventricle of the heart. Nothing abnormal was noticed in the liver or the intestine. Nothing could be ascertained as to the previous history of the woman.

In removing the abdominal viscera the left kidney was noticed to be hydronephrotic, and the ureter was felt to contain small elastic-feeling bodies which collapsed on pressure.

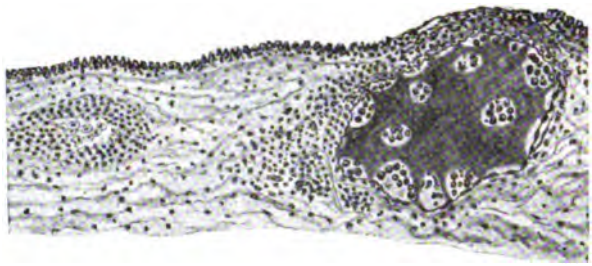
The left kidney was found to contain a group of small cysts at its upper end. In the dilated pelvis of the kidney and in the upper half of the ureter there were numerous cysts of a greenish-brown colour, and being on an average the size of hemp-seed. There was a moderate amount of hydronephrosis. There were numerous small cysts at the neck of the bladder and at the vesical orifices of the ureters. There was one subcapsular cyst in the right kidney, which, in other respects, appeared to the naked eye to be normal.

The contents of the cysts of the ureter in the fresh state were brownish, and showed under the microscope large and small, oval and irregular, cells, which contained bright globules. Some of the globules were free, and they, like those contained in the cells, stained readily with gentian-violet, logwood, &c. No encysted forms were seen. After hardening in alcohol, prismatic crystals, which I have not had leisure to investigate, formed in the cysts. Portions of the left kidney and ureter, and of the affected part of the bladder, were hardened in Müller's fluid, embedded in celloidin, and cut.

Most of the cysts of the ureter had, under a low power, an appearance similar to that represented in Plate IV, fig. 1. The epithelial lining consists of a double row of cubical cells, and the contents of albuminous material in which are imbedded oval cells, with distinct nuclei, and for the most part of large size. It may be seen at a glance that the case is of the same nature as Mr. Eve's. Many of the cysts, however, had contents of a totally different appearance. There was the same albuminous substance, which, in hardening, had shrunk from the epithelial lining except at certain points, but instead of large oval nucleated cells small non-nucleated granular

corpuscles occupied the clear spaces. This appearance is shown in the woodcut.

FIG. 5.

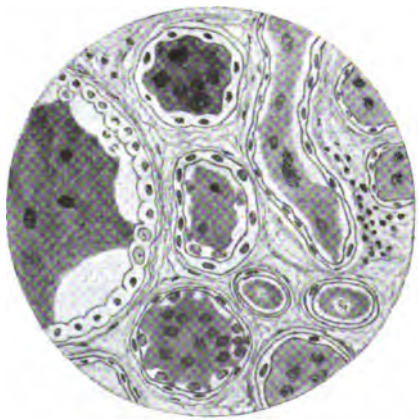


A part of the mucous membrane of the ureter with a cyst to the right, and to the left a mucous crypt in section. Around the cyst is some small cell-infiltration. The epithelium is reduced to a single layer of flattened cells at some parts, and at another heaped up from proliferation. (Zeiss, obj. A, oc. 2.)

A section of the kidney showed the same two forms of cystic distension of the tubules. Some of the smaller (looped) tubules were distended by single oval cells, as is shown in Fig. 6.

The blocking of tubules was much more widespread than was

FIG. 6.



A section of the base of one of the pyramids of the left kidney. There are various cysts containing numerous psorosperms embedded in albuminous material, and single psorosperms in the looped tubules. (Zeiss, obj. F, oc. 2.)

evident to the naked eye. In some parts of the section examined the tubules were free from albuminous contents. In these parts the interstitial tissue was seen to be excessive in amount, and the epithelium was detached from many of the tubules—conditions due to the same pressure that determined the hydronephrosis. In many of the distended tubules hæmatoidin granules were present in the albuminous contents, proving the occurrence of hæmorrhage —a marked symptom in Mr. Eve's case. In many of the smaller tubules albuminous material was arranged in concentric lamellæ about a nucleus.

Examination of the cysts in the bladder gave a negative result, though these and their contents, to the naked eye, exactly resembled those in the ureter. I attribute this to the fact that the sections were cut without embedding, and I now have little doubt that the cysts in the bladder are of the same nature as those in the kidney and ureter.

Such is a general view of the histology of the case; enough, perhaps, to enable one familiar with similar conditions to recognise the case as one of psorospermosis. For my part it was a long time before I could prove that the various cell-forms were indubitably psorosperms, as I am now convinced they are.

Although a parasitic origin of the disease was made probable by the repetition of similar lesions in three separate parts of the urinary tract, by the resemblance of the large nucleated and the smaller granular corpuscles to certain forms of psorosperms in the rabbit's liver and elsewhere, and to those figured by Virchow in the bat's kidney, and by many other considerations, it remained to be absolutely proved that there was here more than a close simulation of psorosperms. To begin with, in none of my preparations could I find distinctly encysted forms such as are found abundantly in the rabbit's liver, and as are figured by Virchow in the plate mentioned above. Very delicate capsules were present around some of the large oval cells. I was able later on to refer them to the epithelial cells. Melassez describes ('Journ. de la Méd. Expt.,' January, 1891) similar delicate capsules in rabbits' psorosperms, and refers them to the same source. I was unable to attempt making cultivations, and apart from these I had to rely on histological appearances. In the first place it was necessary to exclude the possibility of the large size of the egg-shaped cells being due to degeneration. That it was not fatty degeneration

was proved by the action of osmic acid on fresh specimens. In these the large cells were only slightly blackened, not even so much as Melassez describes in rabbits' psorosperms.

Those of the large cells which contained clear drops might have been changed by colloid degeneration. This, however, was made improbable by the great variety of shapes assumed by the drops, some of which were rounded, others irregular, some again free in the albuminous material, as they are represented in Plate IV, fig. 5. The clear bodies in the largest cells are of definite rounded outline. The idea of degeneration was, however, completely dismissed by the discovery of the cell represented at the upper part of fig. 2 of the same plate. The cell has an extremely large nucleus, with a well-marked network and nucleolus. The structure is not that seen in the common vesicular perinuclear degeneration of epithelial cells, and to my mind is incompatible with anything save a perfect state of vitality of the cell, which has the appearance observed when mitosis is about to begin. I could, however, find no mitotic figures, though some of the epithelial cells had double nuclei, as in Fig. 6 on page 96. The two cells at the lower part of Plate IV, fig. 2, show the clear outer zone so frequently present in psorosperms. It now only remained to show that some of the cells were growing within epithelial cells. By rapping on the cover-glass of one of the preparations with the handle of a needle, and in this way causing the albuminous material to crack, the thin capsule of one of the large cells was ruptured (Plate IV, fig. 3). In the same field were two similar large cells contained within greatly distended epithelial cells, which are still in connection with the epithelium of the cyst-wall. Thus the peg-like processes of the albuminous contents of the cysts and the delicate ruptured capsule can be referred to the epithelial cells. After carefully considering and drawing this part of one of the sections, I was convinced that I was in the presence of parasites within epithelial cells.

The appearance of the clear intra-cellular bodies could now be safely referred to endogenous spore-formation, and the parasites to the group of sporozoa. Further, the small free corpuscles already referred to (Fig. 5, page 96) could be justly regarded as free amœboid psorosperms. They are represented on a larger scale in Plate IV, fig. 4. Some of them were free in the areolar tissues outside the cyst. A possible course of development of this amœboid form is suggested in Plate IV, fig. 5—taken partly from forms

DESCRIPTION OF PLATE IV.

Illustrating Mr. J. Jackson Clarke's case of Psorospermosis. (Page 94.)

From drawings by the author.

FIG. 1.—One of the cysts of the ureter drawn under a low power (Zeiss obj. A, oc. 2). The parasites vary greatly in size: they lie in spaces in an albuminous material which has shrunk a little, but remains attached to the lining epithelium by several pointed processes. There are two empty spaces from which psorosperms have escaped.

FIG. 2.—Three psorosperms. The upper one has a very large nucleus with a well-marked reticulum and nucleolus. The other two have a clear outer zone of protoplasm. (Leitz obj. $\frac{1}{10}$ in., Zeiss oc. 2.)

FIG. 3.—Part of a cyst at the margin. The supporting fibrous tissue, the lining epithelium, and several psorosperms are shown. To the left the albuminous material is cracked across, leaving a crevice into which the broken capsule of one of the psorosperms projects. The capsules of the two of the remaining psorosperms are evidently epithelial host-cells. (Zeiss obj. F, oc. 2).

FIG. 4.—Part of the section represented in Fig. 5 on p. 96 in the text, under a higher power (Zeiss obj. F, oc. 2). The epithelium lining the cyst is reduced to a single layer of flattened cells. Both inside and outside the cyst are non-nucleated amœboid psorosperms.

FIG. 5.—Five psorosperms. In the largest are a number of oval "spores;" the remaining four form an ascending series both in size and in complexity of structure. (Zeiss F, oc. 2.)

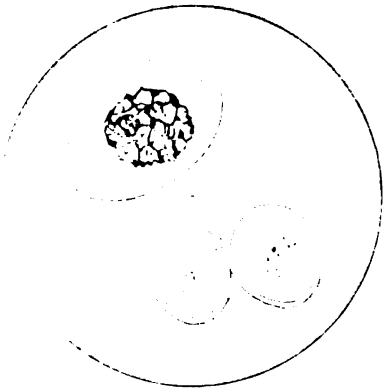


Fig. 2.

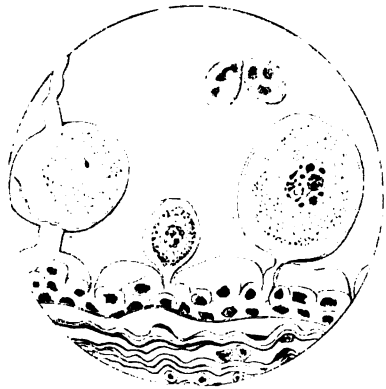


Fig. 3.

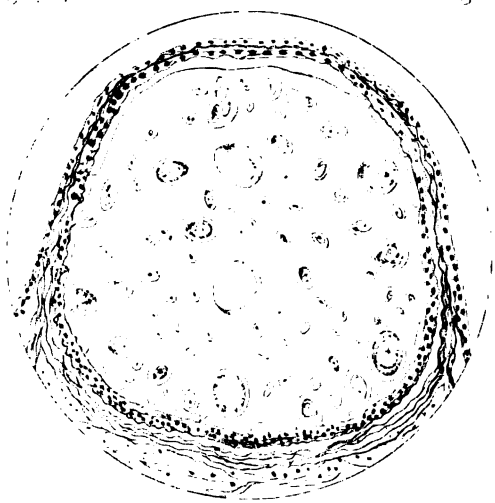


Fig. 1.

Fig. 4.

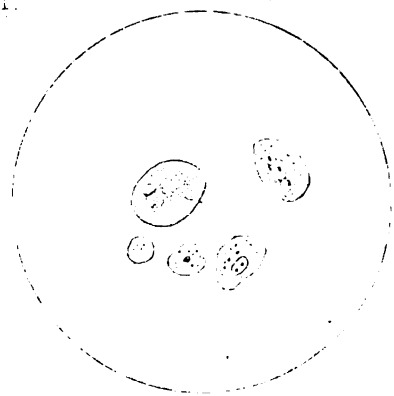


Fig. 5

J. J. Beccle, del. Mintern Bros. sc.

occurring in the cyst represented in Fig. 5 on page 96, and partly from an adjacent cyst in the same section.

I may observe that the free corpuscles represented by Lindemann in a section of kidney, correspond exactly with these amœboid psorosperms; and the concentric corpuscles he also met with, and compared to corpuscles of Hassall, are similar to psorosperms present in parts of the section of the kidney in this case. The appearance is evidently due to the protoplasm having undergone concentric cleavage. I believe Lindemann's case is one of psorospermosis. The slight differences between the histological account of Mr. Eve's and that of the present case may be easily explained. From the figure accompanying the account of the former case, I should say that the epithelium had disintegrated, whilst the psorosperms had in a characteristic manner resisted decomposition. I regret I was not able to obtain the clinical history of Dr. Lees's patient. But there are in the kidneys evidences of hæmorrhage, so marked a symptom in Mr. Eve's case. The mode of death, by cerebral hæmorrhage, points to a high arterial tension. The left ventricle of the heart was greatly hypertrophied.

Many points yet remain unfinished in the examination of the present case, especially with regard to the extent of the affection of the kidneys and bladder, also the nature of the albuminous material, which does not behave like a mere detritus; and the crystals deposited in the cysts call for further investigation.

It is to be hoped that good clinical histories of similar cases may be forthcoming, and then, with that of Mr. Eve's case, they may form a basis for the recognition and study of the condition in life. *February 2nd*, 1892.

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6. *Pigmentation of the glans penis in the negro after circumcision.*

By Samuel G. Shattock.

The specimen which forms the subject of the present notice is one in the Museum of St. Thomas's Hospital. I have thus described it in the new pathological catalogue in course of publication:

"The penis of a negro, of which the integument is much thickened, and has a rugose or corrugated, or, in places, a warty surface. The changes are most marked anteriorly; here the integument is 1¾ inches in thickness. It is noteworthy that the mucous membrane of the glans, which has been exposed by circumcision, has become pigmented so as to resemble the skin."

Microscopic sections of the glans show that the deeper cells of the epithelium, which is of the stratified kind like that of the skin or buccal mucous membrane, are thickly filled with fine granules of yellowish-brown pigment. The pigment is in chief amount in the deepest or vertical set of cells, but it is not absolutely confined to these. The coloration is not uniformly distributed, being more marked in some situations than in others.

In no inconsiderable numbers there occur groups of similar granules free between the bundles of the connective tissue of the corium; here and there the granules are clustered about the nuclei of connective-tissue cells, and probably lie in the cell protoplasm.

The resemblance between such sections and others of the skin itself is very close. In the skin the chief portion of the pigment lies in the vertical or deepest set of the epidermal cells, though it is not confined to these; and, as in the corium of the glans, so in that of the skin, there occur groups of pigment granules free or congregated about cell nuclei, and probably within the bodies of cells.

I should believe that the latter pigment is of the same kind as that within the epithelium, for no red blood discs, from which it might be derived, are discernible in the clefts of the connective tissue; and though there are groups of leucocytes about the vessels in both the superficial and deeper parts of the thickened integument, such free groups of pigment are limited to the portion of the corium in the immediate vicinity of the epidermis.

Remarks.—It will appear from the foregoing observation that the exposure of the glans by circumcision leads to the pigmentation of the deeper cells of the epithelium as well as to the dry, horny condition of its superficial elements, and thus brings about so close an imitation of the skin as to show that there is no real difference between the two.

This is perhaps the very simplest degree of the process which Virchow has named metaplasia, or the transformation of one variety of tissue into another.

Connective tissue is never transformed into epithelial, if we limit

this term to tissue of epiblastic or hypoblastic descent, nor is epithelial into connective tissue; but apart from this the various forms of connective tissue are mutually interchangeable, *e. g.* connective tissue into cartilage, and either of them into mucous tissue; connective tissue into bone; and bone, after decalcification, into connective tissue, as occurs in osteomalacia ('Path. Soc. Trans.,' vol. xxxviii, p. 170).

And under the same term of metaplasia we may include the transformation of one variety of epithelial tissue into another. Some such mutations occur in the course of development, but others under special circumstances are witnessed in the adult. The very best instances are such as are seen in complete inversion of the uterus, when the inverted part projects from the vulva; the columnar-celled investment under these circumstances becomes a stratified squamous one: or such as that recorded by Dr. Gervis in the Obstetrical Society's 'Transactions,' vol. xxviii, 1886, in which a uterine myoma partially projected into the vagina; here the epithelium over the intra-vaginal part of the tumour had undergone a change from the columnar into the stratified squamous kind, the cells lining the glands of the extruded part retaining their normal columnar characters. In the thirty-fifth volume of the Society's 'Transactions,' 1884, Mr. Roeckel records a series of observations he made on a similar change of epithelium on internal piles that had long remained extruded from the anus; the columnar epithelium became transformed into the stratified squamous kind like that of the common integument, or of the terminal part of the rectum. And a similar change has been observed by Mr. Sutton two years after colotomy, in the mucous membrane extruded at the artificial anus. But the nearest example to that under notice is one recorded by Dr. Barnes in the thirty-fourth volume of the Society's 'Transactions.'

It was that of a Hindu woman suffering from hypertrophic elongation of the cervix uteri; the lower part of the cervix projected from the vulva, and, as in the negro, so here the epithelium of the exposed portions of the mucous membrane became black like the general integument.

It might be presumed from these facts that the general result of circumcision in the black races was to induce pigmentation of the glans. On this point Prince Orisadipe Obasa, of Ikija, Lagos, West Africa, lately a student at St. Thomas's Hospital, was good

enough to obtain for me the following information, which is all that could be desired.

In children before circumcision the glans penis is of the colour of ordinary mucous membrane. Soon after circumcision it commences to become pigmented; the pigmentation proceeds until the glans becomes nearly, but not quite, as deeply coloured as the skin of the penis; if it ever becomes as deeply pigmented as the skin, this is rare.

In uncircumcised adults, the glans retains much of the appearances observed in uncircumcised children, but it is slightly darker, and this varies with the amount of exposure; but it is only after circumcision that the glans becomes at all deeply pigmented.

In uncircumcised children who are allowed to run about naked, the glans is always darker than in those of the same age who go about clothed.

It is surely remarkable that in the lifetime of the individual a part, which is naturally almost unpigmented, should on exposure become black like the rest of the integument. Does the readiness with which this takes place indicate that the general epidermis originally possessed the same capacity, and that the black colour of the race is not to be explained merely by the action of environment, but implies also a special tendency to variation in this particular direction which is not possessed in the same degree by white races? The view, indeed, that the differences in coloration of the skin could be accounted for by long exposure to different climates has been generally rejected because, writes Darwin,[1] the distribution of the variously coloured races, most of whom must have long inhabited their present homes, does not coincide with corresponding differences of climate. "Some little weight may be given to such cases as that of the Dutch families, who, as we hear on excellent authority, have not undergone the least change of colour after residing for three centuries in South Africa."

The pigmentation, it may be assumed, then, was in the first instance a variation, and this I imagine to be borne out by the facts recorded in the present note.

Darwin offers in different places two distinct suggestions to account for its universality in particular localities, though admitting that there is little evidence for either.

Not to digress further, these are: (1) that dark races might have

* 'The Descent of Man,' pt. 1, chap. vii, 2nd edit.

acquired their tints by the darker individuals escaping from the deadly influence of the miasma of their native countries during a long series of generations; (2) that they might have acquired their colour through sexual selection. *December 1st*, 1891.

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7. *Primary (?) malignant growth of the root of the penis.*

By E. Hurry Fenwick.

In 1890 I showed at one of the meetings of this Society a somewhat unusual specimen of sarcoma of the capsule of the left crus penis.

As a contrast case I wish to draw attention to a very rapid and malignant growth, which apparently commenced at or near the bulb. The patient, aged 47, was taken into the London Hospital under my care on September 12th, 1891, with hæmaturia and persistent priapism. He stated that ten days previous to his admission, being then in perfect health, he was struck forcibly in the crutch by the sudden shifting of a piece of iron over which he was stooping straddlewise. Ten minutes afterwards he felt sick and passed bloody urine. He went home and to bed, suffering severe pain across the lower part of his belly, with a frequent desire to micturate, but experiencing great difficulty in voiding urine. The bleeding continued. Three days after the blow the penis began to swell on the left side, and he had pain referred to a spot situated an inch from the meatus. The organ gradually got larger and curved to the right, in which condition he was first seen by myself.

Present condition (fourteen days after the accident).—"Penis enormously swollen, curved to the right groin. The left corpus cavernosum is occupied by a row of hard knotty masses which are exquisitely tender. The left side of the perinæum in the neighbourhood of the bulb is swollen and lumpy, being similar in this respect to the left corpus. He is very anæmic, but well nourished; he is passing water every half-hour with pain and much difficulty. The urine is very bloody, acid, and contains pus. The temperature is normal. The prostate is of normal size per rectum."

The blood gradually ceased, the difficulty in urination diminished,

but on the 28th September it was noted that the right half of the penis had become involved, and that the penis was quite erect and straight. The small flaccid glans penis was thrust out, uncovered by prepuce, from the enormously distended corpora cavernosa. The implication of the right half of the penis showed the diagnosis of traumatic extravasation of blood into the corpus to be incorrect, and the expediency of performing the Thiersch-Gould operation of removing the penis was discussed, and rejected on account of the acuteness of the malignancy. The following notes are excerpted from the clinical history:

October 7th.—Urine is passed every two or three hours in the day and night. Since the blood has ceased the penis has got still larger; it now measures 11 inches in circumference at the level of the suspensory ligament, and 7 inches midway between the point of the glans and this spot. The swelling in the neighbourhood of the bulb has also increased very greatly, and the entire perinæum is occupied by a knobby hard mass, which measures 6½ inches across from ramus to ramus at the post-scrotal angle. No secondary deposits can be discovered anywhere.

30th.—The dorsum of the penis has become swollen and œdematous; there is increased difficulty in urination, and more tenderness of the penis on pressure.

31st.—On the under surface of the penis there is a suspicious violet mark, as if the growth was going to burst through the skin in this position (tension gangrene).

November 1st.—Gangrene of under surface of penis.

2nd.—Sudden retention, the urethra being closed by inflammatory or neoplastic pressure. A boutonnière was performed and the bladder drained, with great relief.

6th.—The penis has been sloughing freely, and now only a narrow strip of skin is left upon the dorsum to cover a raw stump of erect malignant growth. Perinæum is breaking down and fungating out.

10th.—Amount of urine is beginning to decrease, and the patient is getting weaker.

22nd.—Died two months and three weeks after the blow on the perinæum.

The following are the notes of the *post-mortem*:

Autopsy.—"The penis is merely a gangrenous malignant mass, with a strip of skin along the dorsum. The corpora cavernosa and

corpus spongiosum are transformed into an indescribable slough, in which no trace of the urethra can be found. The same condition is seen in the perinæum, most of this region being replaced by an open fungating sloughy growth. Both ischio-rectal fossæ are filled with the same growth, but here the breaking down is not so marked, and the whitish colour of the softish carcinoma is plainly visible. The prostate is untouched, but the membranous urethra is surrounded by small pea-sized deposits of growth, and its wall is infiltrated with the same material. The bladder is small, but no part of its structure is implicated. The left kidney is healthy. On the right side of the spinal column, and firmly attached to it, opposite the position of the left kidney, is a huge soft carcinomatous mass which weighs, on being dissected away, 3 lbs. 3 oz. Apparently it springs from the glands in this situation and has grown outwards, for the right kidney is entirely transformed into carcinoma, and is almost lost in the *outer* edge of the tumour. There is, however, a thin line of secreting structure left, which would correspond to the upper rim of the kidney. No calculi can be found, either in the position which should have been occupied by the renal pelvis, or in any portion of the tumour. The vena cava is so compressed that its calibre is occluded, and in the right lobe of the liver are a few small deposits, and a few also are found in the under surface of the right lower lobe of the lung. The other organs in the body are healthy and call for no remark."

There are several points of interest in this case:

1. From the literature it will be gathered that growth of the corpora cavernosa commencing in the region of the bulb is of rare occurrence.

2. The appearance of the growth in the left corpus followed almost immediately after the blow upon the crutch.

3. The entire course of the disease was extremely rapid. (Compare 'Path. Trans.,' 1890, p. 194.)

4. It is difficult to say with certainty which was the exact site of the origin of the epithelioma. It was reasonable to suppose that a careful microscopy of the tumour would settle this question, but it has not. Mr. Targett, who kindly examined a large number of sections prepared from various parts, reports that it is a squamous-celled epithelioma. This fact would indicate either an urethral or a renal origin, for cases of renal squamous epithelioma have been

placed on record. If the former view, which I am inclined to adopt, be accepted, then we might ask, why did the *left* abdominal glands escape when the first visible growth appeared in the *left* side of the root of the penis? On the other hand, if the penile growth is looked upon as being secondary to a latent renal epithelioma, then it is instructive to note the effect of traumatism in localising and concentrating a secondary deposit.

May 17th, 1892.

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8. *Acute, double, tubercular disease of the bodies of the testicles.*

By Gilbert Barling, M.B.

Both organs, but especially the left, were considerably enlarged. In the left were several patches of caseous and diffluent material, in the right there was one large softened area; these were entirely limited to the bodies of the testicles. In addition to the caseous patches there was a marked fibrosis surrounding them. Tubercle bacilli were found in preparations from the caseous parts, but there were no well-defined giant-cell systems.

The testicles were removed from a patient, aged 31, who asserted that he was in good health until September 15th, 1891, when in making a violent effort he overstrained himself and hurt his testicles, which began to swell in a few hours. When seen some five weeks afterwards the testicles were both swollen, painful, and tender, the scrotum was slightly œdematous, and there was a little fluid in each tunica vaginalis. The temperature was of the hectic type, ranging from 103° in the evening to normal or subnormal in the morning. The parts about the base of the bladder were healthy, but there was a suspicion of phthisis at the right apex. There was no history or evidence of syphilis.

Some weeks later the temperature in the evening rose only to about 100°, and the local condition was less acute, but at the end of nineteen weeks from the injury double castration was performed, to prevent extension to other parts of the genito-urinary tract, and to rid the patient of the painful encumbrances.

April 5th, 1892.

9. *Parepididymal cyst.*

By Samuel G. Shattock.

[With Plate II, fig. 1 (see page 52).]

The right testicle of an adult, with the spermatic cord, &c. Lying immediately behind the testicle and epididymis, and between these and the vas deferens, is a large thinly-walled loculated cyst about 3 inches in length. It overtops the globus major by 1½ inches, and reaches inferiorly as far as the lower end of the testicle.

In addition to the chief cyst there are three much smaller, which lie in front of its anterior wall. The spermatic vessels pass over the posterior and inner side of the main cyst, to the hilum testis, the vas deferens directly behind it, and finally below it, to reach the globus minor.

The body of the testicle and the whole of the epididymis are perfectly normal, and there is a well-formed hydatid of Morgagni projecting from between the globus major and summit of the testicle into the tunica vaginalis; the sac of the latter is quite distinct from the cyst, and is normal both in size and disposition (Museum, St. Thomas's Hospital).

Remarks.—The position and relations of this cyst render it evident that it must be regarded as having arisen in connection, not with the Müllerian duct, but with certain of the tubuli of the Wolffian body.

It will be remembered that in the male the Wolffian duct forms the tube of the epididymis, the vas deferens, and ejaculatory duct; certain of the tubuli of the Wolffian body persist, as the coni vasculosi and tubuli efferentes, whilst outgrowths from the Malpighian corpuscles of the Wolffian body produce the rete testis, or tubular structures in the hilum of the testicle.

But there persist, also, the functionless relics of other Wolffian tubules, which appear as vasa aberrantia and the organ of Giraldés. The latter term is limited to the small collection of obsolete tubuli which lie above the globus major in front of the cord, and beneath the parietal layer of the tunica vaginalis. The vasa aberrantia of Haller are one or more convoluted diverticula leading from the lower part of the canal of the epididymis, or the commencement of

the vas deferens; such aberrant diverticula may extend an inch or more upwards amongst the vessels of the cord.

In their relations the cysts under notice correspond precisely with one or more of such vasa aberrantia, and such an origin will fully explain them.

Although the main cyst overtops the globus major, it is not necessary to suppose that the tubuli of the organ of Giraldés are concerned together with a vas aberrans; for a dilatation sufficient to cause the circumferential increase implied by the size of the cyst, would lead to a corresponding elongation in the vertical direction enough to account for the height to which the cyst rises.

So, too, are explained, viz. by the dilatation of such a tortuous tube as a vas aberrans, the multilocular character of the chief cyst and the presence of its smaller subdivisions. I have named the cyst parepididymal because, like the organ of Giraldés, such vasa aberrantia are remnants of Wolffian tubuli related to the epididymis, and not to the body of the testicle.[1]

The existence of a normal hydatid of Morgagni projecting from the fissure between the globus major and summit of the testicle disposes, perhaps, of the supposition that the cyst may have arisen in the Müllerian duct. An example of persistent Müllerian duct in the male has been lately put on record by Mr. Lockwood.[2] This resembles the well-known case of Dr. Ord's[3] in that the dilated duct is connected superiorly with the kidney, and descends thence towards the prostate.

Mr. Lockwood's case is highly interesting since the hydatid of Morgagni was absent on the side of the malformation, though well developed on the other.

In Dr. Ord's case (the specimen of which is in the Museum of St. Thomas's Hospital) circumstances prevented any observation on the testicle.

Dr. Ord refers in his paper to another case noticed in the 'British Medical Journal' of September 6th, 1879, as having been examined by Ch. Rémy, and published in the 'Journal de l'Anatomie et Physiologie,' 1879. The subject was a boy, aged 6 years,

[1] Henle has designated the organ of Giraldés, the parepididymis, more judiciously than Waldeyer, who has named it the paradidymis.

[2] 'Proceedings of the Anatomical Society of Great Britain and Ireland,' November, 1891.

[3] 'Med.-Chir. Trans.,' vol. lxiii.

and the malformation was unilateral. The upper end of the persistent Müllerian duct was related superiorly with a collection of cysts close to the adrenal, supposed to be remains of the Wolffian body; and it opened inferiorly into the utriculus masculinus. The hydatid of Morgagni was present, as large as a millet seed, on the same side as that on which the duct was persistent, and, curiously enough, was wanting on the opposite side.

On Waldeyer's carefully elaborated view that the hydatid is the end of the Müllerian duct, this case is inexplicable. There are, as is known, other "hydatids" of similar appearance to that of Morgagni, which are directly related to the globus major, and connected in descent not with the Müllerian duct but with Wolffian tubuli such as those from which the coni vasculosi are formed, Yet the figure illustrating the original paper represents the hydatid as lying between the globus major and body of the testis, and so as having the proper position of the true structure. Some may be incredulous enough to suppose that an erroneous transposition of right and left has crept into the account, and failing a personal inspection reject the case as it at present stands.

Rémy reports that J. A. Boogard relates the case of a man, aged 66, in whom there was a persistence of both Müllerian ducts, these being unequally enlarged.

Boogard has, but with little reason, thought of relating such unnatural persistence with the avine condition in which only the left Müllerian duct is permanent. In the human subject, however, the side of persistence is variable; moreover, both ducts may persist;[1] nor is it held by philosophical zoologists that birds have intervened in the line of mammalian descent, and if this is so no just comparisons can be made in the special morphology of these two classes.

It is remarkable that in all the cases cited the upper end of the persistent Müllerian duct retained a connection with the kidney, in place of having migrated with the testicle into the scrotum, an occurrence for which no satisfactory explanation has been offered.

In the Museum of the Royal College of Surgeons, London, I find two preparations similar in kind to that under notice. No. 247 shows a globular cyst about three quarters of an inch in

[1] Ch. Rémy states that Dr. E. Martin has observed a case of persistent Müllerian ducts in the fœtus accompanied with arrested development of nearly all the genito-urinary organs. In Boogard's own case the same was true.

diameter, situated immediately behind the middle of the posterior margin of the epididymis; the vas deferens passes over the back of the cyst, and there is present a true hydatid of Morgagni; the preparation is figured in Sir A. P. Cooper's 'Observations on the Structure and Diseases of the Testicle,' part ii, pl. xiv, fig. 2, London, 1830. But there is another preparation in the same museum more closely resembling the one in St. Thomas's—No. 4291 (Hunterian)—a testicle to the posterior part of which, but external to the tunica vaginalis, is attached a large cyst which contained a serous fluid; the cyst is 3 inches in length; the relation of the vas deferens is not shown, and as the cavity of the tunica vaginalis is mostly obliterated, the relations of the cyst to the epididymis are not clearly recognisable.

The fact that collections of fluid occur "in the connective tissue of the tunica vaginalis" was known to Hunter, according to a quotation given under the preparation in the College catalogue.

Cases of this kind would probably be diagnosed clinically as vaginal hydroceles arising in connection with a semi-rotated testicle; the testicle lies at the lower part, but in front of the sac.

As to whether the contents of such cysts are sperm-holding, like those arising in the globus major, no evidence is forthcoming; probably they would not be so, any more than cysts arising in the organ of Giraldés.

Are there any analogous cysts in the female? This I think is so, although the analogy has not as yet been definitely stated.

Adopting the nomenclature which makes the paradidymis, represented by the functional rete testis, or tubular structures in the hilum of the testicle formed from the Wolffian body, correspond with the paroophoron, represented by similar but functionless outgrowths of the Wolffian body into the hilum of the ovary, the epididymis will correspond with the epoophoron (parovarium) of the female.

Now Mr. Doran, in his careful monograph on 'Tumours of the Ovary, Fallopian Tube, and Broad Ligament,' refers in more than one place to cysts of the broad ligament which originate, not in those vertical tubuli of the epoophoron (parovarium) which converge towards the hilum of the ovary and are represented in the male by the coni vasiculosi and tubuli efferentes, but in tubuli connected with the subjacent Wolffian duct, but which lie between the ovary and the uterus. Such tubuli may be compared in their

relations with vasa aberrantia of the male, which, in a similar way, are Wolffian tubuli arising from the Wolffian duct, but are unlike those which produce the coni vasculosi in having no permanent connection with the testis. If this be admitted it will entail the introduction of yet another addition to the list of sexual structures in the female. Such Wolffian tubuli in the female as do not form part of the proper epoophoron (parovarium) may be designated collectively as the parepoophoron, a term framed on the lines of parepididymis, which later may be used to include not only the organ of Giraldés or those tubuli above the epididymis, but other tubuli (vasa aberrantia) arising from the Wolffian duct at a lower level. So cysts of the broad ligament arising in such will be parepoophoral, as distinguished from epoophoral or parovarian.

May 3rd, 1892.

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10. *Pregnant uterus bicornis.* (*Card specimen.*)

By J. R. Ratcliffe, M.B.

The uterus was from a woman killed by a crane accident. The uterus has two large horns separated by a high recto-vesical fold. The horns are almost the same size, and the left contained an embryo.

The corpus luteum was in the right ovary. The vagina is large, and shows a superior and inferior ridge.

The right non-pregnant horn showed great hypertrophy of the mucous membrane. *May 3rd*, 1892.

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11. *Malformation of uterus.* (*Card specimen.*)

By H. W. G. Mackenzie, M.D.

A one-horned uterus. The right horn is represented by a nodule of muscular tissue on the Fallopian tube about 2 inches from the uterus. The left tube leaves the uterus near

the fundus, the right one in the neighbourhood of the internal os.

From a woman, aged 28. No children. Death from ulcerative colitis from a malignant stricture of the colon.

October 20th, 1891.

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12. *Cystic disease of the breasts.*

By Raymond Johnson, M.B., B.S.

H. K—, a single woman, aged 33, was admitted into University College Hospital, under the care of the late Mr. John Marshall, on November 2nd, 1877. Her general health was good, and she menstruated regularly. For eighteen months she had suffered from occasional pricking pain in the left breast. Later the breast was said to have become of a dark-purplish colour, and there was frequently a "black" discharge from the nipple. The breast is described as follows:—"At the central part, but chiefly in the upper and outer side, is a tumour the size of a large orange, not adherent to the skin; there are no enlarged veins over it; it is quite free from the surface of the pectoral; the tumour is nodular, the projections being evidently cysts; its outline is fairly defined. The other parts of the breast feel cordy. At the lower and outer part of the breast is a pedunculated nodule the size of a nut. No enlarged glands in the axilla or posterior triangle. On compressing the tumour firmly a peculiar crackling is felt, and a brownish-red fluid escapes from the nipple, which is not retracted."

On November 6th, 1877, nine drachms of dark red fluid were withdrawn by puncturing the large cyst. The whole breast was excised, free suppuration occurred, and the wound had healed in a month. The condition of the breast is thus described:—"The inner wall of the large cyst is irregular, fibrous bands projecting from its surface; it contains a polypoid mass as large as the thumb. There is a smaller cyst in the centre of the breast, and numerous others as large as peas scattered through it. The nodule felt at the lower border of the breast is evidently an adenoma.

There are several firm nodules throughout the breast; the smaller cysts are evidently connected with these, as in several cases the nodules and cysts are conjoined. The cysts are lined with cubical epithelium; the nodules consist of fibro-adenoma."

Four and a half years later, in April, 1882, the patient was re-admitted to the hospital. In 1880 small hard lumps were noticed in the right breast; these had slowly increased in size. It is noted that menstruation had become painful and scanty. The scar in the left mammary region was sound. The right breast is thus described:—"It is not enlarged, but the skin is slightly raised just outside the nipple. The whole breast is rendered knotty by small nodules as large as peas. The largest nodule, which raises the skin, is as large as a haricot bean. The nodules show a general tendency to radiate in strings from the nipple. There are two or three slightly enlarged glands in the axilla."

On April 22nd, 1882, the whole breast was excised.

In 1889 the patient was again admitted, under the care of Mr. Marcus Beck. Both scars were quite healthy; above the middle of the left scar was a rounded moveable swelling an inch in diameter; it had been slowly forming for two years. It was smooth and elastic, and unattached to the skin. An incision was made over it, and a cyst with dark fluid contents opened. The cyst was excised together with a broad margin of surrounding fat.

The cyst, which in the recent state was as large as a small chestnut, is partially filled by a soft papillomatous growth, attached by a narrow pedicle to the wall of the cyst. Adjacent to this cyst is a smaller one, filled by a similar growth as large as a pea. In the fat around the cysts are a few strands of dense white tissue. This tissue was examined microscopically. It contains breast tissue showing all the stages of cyst formation, in which the acini rather than the ducts seem to be concerned. The epithelium lining the spaces is for the most part composed of several layers of rounded cells, but in some cases forms a single layer of low cubical cells. The largest spaces have colloidal contents. In some spaces small bud-like growths spring from the wall. These are for the most part probably the remains of septa between dilated acini which have coalesced. The cystic gland tissue is mixed up with dense fibrous tissue and a quantity of fat.

Two questions require consideration:—What is the nature of the disease? How can we explain the recurrence? In the case of

each breast the disease has been described in the Hospital Reports as "cystic adenoma."

In the case before us, however, the essential change seems undoubtedly to be a cystic degeneration of the gland tissue. The presence in some of the cysts of intra-cystic growths in no way affects the question. It is clinically convenient and pathologically necessary that we should restrict the use of the term adenoma, as insisted by Mr. Beck, to an encapsuled tumour of the breast of which the glandular tissue forms an essential part; it matters not whether this glandular tissue retains a more or less typical structure in the one variety, or appears in the form of large spaces filled with intra-cystic growths in the opposite extreme.

Cystic disease of the breast tissue proper conveniently divides itself into two chief classes—that in which a single cyst arises from the dilatation of a duct or acinus, and that in which a cystic degeneration more or less extensively affects the whole organ. Of this latter class we have two varieties, according to whether the gland affected is in its period of activity or in a state of involution; and in each variety the spaces may or may not contain intra-cystic growths. The case before us is an example of cystic disease of the active breast with formation of intra-cystic growths.

According to one view as to the origin of the adenomata, these tumours are related to cystic disease, in that an adenoma is believed to be an intra-cystic growth which, completely filling the space in which it grows, comes to be a solid encapsuled tumour. If such a mode of origin be the usual one we should expect that such tumours would be frequently multiple and situated in the substance of the gland, that they would occur at the age most common for cystic disease, and that a history of blood-stained discharge from the nipple would not be unusual; whereas experience shows that they are usually single and peripheral, that they occur most commonly between the ages of twenty and thirty, when cystic disease is rare, and that a history of discharge from the nipple is very unusual.

I have twice stained the inner surface of the capsule of an adeno-fibroma with nitrate of silver, but have failed to demonstrate any epithelial lining, which should be present if the capsule is really a cyst-wall. The usual position of these tumours, on the surface or at the periphery of the breast, strongly supports the view that they arise in small outlying lobules.

The point of chief interest in the case before us, is the fact that recurrence of the disease took place in the left mammary region ten years after the breast had been excised. Viewing the case as one of cystic degeneration, one can only explain the recurrence as resulting from a similar change taking place in a fragment of breast tissue left behind at the time of the operation. The appearances shown by the microscope, and described above, support this hypothesis, for around the two cysts visible to the naked eye are seen groups of acini undergoing cystic change. The question naturally arises—What was the exciting cause of the cystic degeneration of this isolated fragment of gland tissue after an interval of ten years? I have no answer to offer; but if such disease be parasitic, as seems more than probable, one can only suppose that the organism remained there in some resting form, finally waking again into its active state.

In the usual mode of excision of the breast, especially in cases where the subcutaneous fat is scanty, it is probably common, as in this case, for fragments of breast tissue to be left behind. The surface of the gland is here and there very closely connected with the deeper layers of the skin by the so-called suspensory ligaments of Sir Astley Cooper, and it is especially at these points that gland tissue is likely to be divided in reflecting skin flaps from its surface. In this case there can be no doubt that the recurrence of the cystic disease is thus explicable; and I am strongly of opinion that a considerable number of cases of local recurrence of carcinoma after excision of the breast receive a like explanation, especially such recurrent nodules as occur around the scar in the mammary region, and beneath, rather than in, the skin.

October 20th, 1891.

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13. *Cystic fibroma of breast weighing* 8 *lbs.* 7 *oz.* (*Card specimen.*)

By Alban Doran.

Removed from a healthy woman, aged 69. The tumour had been growing for four and a half years, recently very fast. It formed a very large swelling, which replaced the left breast and

projected upwards so as to lie in front of the clavicle. The surface was irregular. Large veins ran over the upper part, whilst over the lower were ecchymoses and patches of varicose veins: the skin was here deep red, but not adherent to the tumour. The nipple was flattened and stretched over the tumour. There were no enlarged glands in the axilla. The right breast was atrophied. I removed the tumour on June 25th, 1891; there were very large vessels which required ligature. The wound healed rapidly, and the patient left the hospital in excellent health. A month later she died after an operation for strangulated femoral hernia; no trace of malignant disease was discovered after death.

The tumour is firm on section, and consists of numerous cysts occupied by foliate masses of fibrous tissue which project into them from one point in their walls and fill them. The semilunar cavities seen in parts of the cut surface represent portions of cysts not completely filled by the solid growths.

The microscope shows that the cystic cavities are dilated ducts of the mammary gland. The tumour substance consists of connective tissue; in some parts the white fibres are abundant and closely packed. *May 3rd*, 1892.

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14. *Duct papilloma of breast.*

By C. B. Lockwood.

The specimen was considered to be one of malignant duct papilloma, or duct carcinoma, of the breast. Its history was as follows:—The patient was an unmarried woman, aged 39, and she first noticed something wrong with the left breast eighteen months before. The left breast was larger and harder than the other, and there was a continuous pain in it, which was occasionally shooting in character. Six weeks ago blood began to exude from the nipple, and the amount increased until she lost about a teaspoonful in twenty-four hours. Examination showed that the left breast was larger than the right, and very hard and nodular. When the largest nodule was squeezed blood ran from the nipple.

The lower axillary glands were slightly enlarged. Under these circumstances Mr. Willett removed the whole mammary gland together with two axillary glands. The patient made a rapid and safe recovery.

When the diseased gland was incised and examined with the naked eye, the section had not the appearance of cancer. A number of apertures with patent lumen and thickened walls were studded over the section; in places, also, the indurated gland had irregular yellow patches in its substance. Histologically the connective tissue of the breast was natural in quality, but interspersed with foci of small cell growth with epithelial cells in their centres. But the most striking features were the dilated ducts. These were lined with elongated but healthy epithelial cells, which in many places formed papillæ which projected into the dilated lumen. These papillæ were solid columns of cells, which united to one another by their free ends. These appearances would not, perhaps, have justified a diagnosis of carcinoma, were it not that in places the proliferated epithelium lining the ducts had invaded the connective tissue of the breast, and this was probably the origin of the epithelial cells which have been spoken of before as being surrounded by small cell growth.

The axillary glands were normal. Thus, taking the clinical and histological characters of this growth together, they were characteristic of an early stage of duct carcinoma. *May 17th*, 1892.

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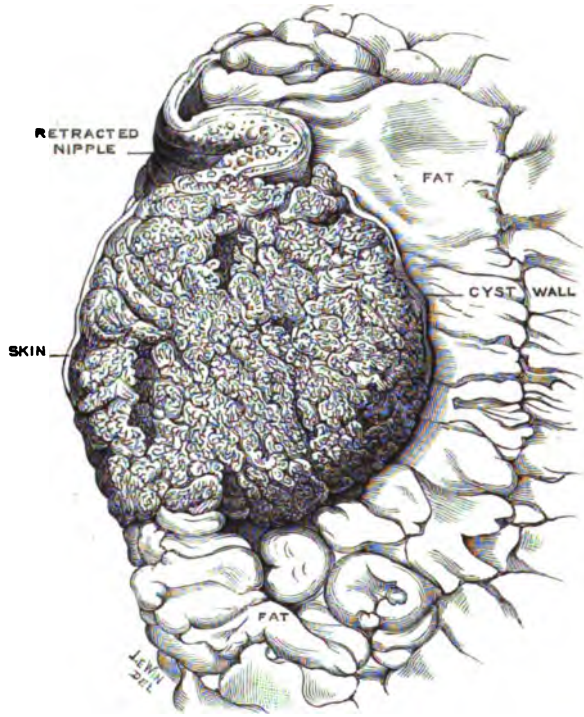
15. *A case of duct papilloma of the breast.* (*Card specimen.*)

By J. Bland Sutton.

M. H—, a tall, stout woman, 68 years of age, the mother of thirteen children, had been aware for two years of the existence of a tumour in the left breast; it had increased in size very slowly, and had never caused pain. During the last six months the patient had been troubled by a free discharge of blood-stained fluid from the nipple, and this of late had been so abundant as to become a source of great inconvenience and discomfort.

When she came under my care the most noticeable features were these:—The left breast presented a tumour the size of a Tangerine orange, situated immediately to the outer side of the nipple, which was retracted. The tumour stood above the level of the surrounding skin, and was of a deep red colour. A small soft tuft of granulation-like tissue, resembling a small ripe mulberry, projected into the bay formed by the retracted nipple, and from this

Fig. 7.



Section of a breast with duct papilloma.

the bloody fluid appeared to ooze. The skin over the tumour was smooth and tense. There were no enlarged glands. On these grounds I had no hesitation in pronouncing the tumour to be a villous, or duct cancer.

The breast was freely removed, and on cutting through the tumour the parts had the disposition shown in Fig. 7. The tumour

was a cyst with a very definite wall, lying immediately beneath the skin, and encroaching upon the nipple. The whole of the cyst was filled with a mass of soft tissue of a deep mahogany colour. When carefully hardened, and subsequently examined, the intra-cystic mass was found to grow from a broad base attached to the portion of the cyst-wall nearest the skin. Near the nipple some of the warty growth had made its way through the cyst-wall into the recess formed by the nipple, and appeared to be the source of the blood-stained fluid.

When examined by the microscope the intra-cystic tissue is seen to be made up of villous processes of great complexity. The wall of the cyst is lined by regular cubical epithelium, but the processes which bud from it are composed of epithelial cells such as exist in warts growing from mucous membrane. In some places the cells are almost columnar, many are pyriform, but most of them are spheroidal. In all parts of the sections the villous processes are solid, and in every respect like sections of compound papillomata.

The anatomy of the tumour indicates clearly enough, that in this case at least the papillomata originated in a pre-existing epithelial-lined cavity. The presence of epithelium on the inner wall of the cyst is quite sufficient to prove that it is not an adventitious capsule. *May 17th*, 1892.

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16. *Columnar-celled (duct) carcinoma of the male breast.* (*Card specimen.*)

By Samuel G. Shattock.

The breast was removed from a man 57 years of age by Mr. Mackellar, to whom I am indebted for its exhibition. The presence of a tumour had been noticed for three years, and was accompanied with a yellowish discharge from the nipple.

The new growth is spheroidal, 2·5 × 1·5 cm. in diameter, and lies immediately beneath, and in close relation with, the nipple. Though bounded by a fibrous capsule and fairly circumscribed, it

is closely adherent to the surrounding tissues; in consistence it is moderately firm, and presents to the naked eye a distinctly alveolar construction.

Histology.—The tumour consists of mutually adapted channels, all of which are lined with a single layer of well-formed columnar epithelium; the channels have a distinct lumen, though this is mostly occupied with secretion, in which lie many leucocytes. Whether the tumour has arisen from the ducts by outgrowth into the surrounding tissues, or has been preceded by the formation of a cyst, is now beyond determination.[1] *May 3rd*, 1892.

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17. *A mamma containing adenomatous and carcinomatous tumours.*

By G. B. M. White.

The patient was admitted into University College Hospital during the past year, under the care of Mr. Beck; she was 61 years of age, unmarried, and had always enjoyed good health.

She gave the following history:—About two years ago she first noticed that the nipple of the right breast began to turn in, and shortly after this she became aware of a lump in the breast. It was quite painless, and increased in size only very gradually. She has had pain in the breast during the last year. During the last week or two the size of the tumour has been increasing rapidly. She has lost flesh considerably during the summer, and the appetite has been very bad. The menopause occurred twelve years ago, and was accompanied with much suffering.

Present state on admission.—In the right breast, just internal to and implicating the nipple, is a hard flattened tumour, rising half an inch above the level of the skin around, and measuring 1½ inches in its longest diameter. On its outer side is a deep pit corresponding to the angle between the nipple and the areola. The skin

[1] See remarks on a specimen of duct carcinoma recorded by the author in the 39th volume of the Society's 'Transactions.'

over the tumour is thin and adherent, and shows many dilated veins. Deeply, the tumour is very firmly fixed to the surface of the breast, and everywhere its border overlaps the surface of the gland. It is thus pedunculated, and it appears to be fixed at the nipple only. It is extremely hard and not tender. Its surface is quite smooth. Other parts of the gland appear to be excessively tender, especially where the breast overlies the rib cartilages. The same thing is noticed in the left breast. The whole gland moves freely over the surface of the pectoral muscle. In the right axilla are some enlarged and hard lymphatic glands; the largest of these lies high up in the axilla, and is freely moveable. There are no enlarged glands above the clavicle.

In the left breast, a little above the nipple, is a small oval swelling, moving freely beneath the skin and upon the surface of the breast. It feels very elastic, but does not give fluctuation. There are no enlarged glands in the left axilla, or above the clavicle. As many as fourteen of De Morgan's spots can be counted upon the front of the chest.

The day after admission the right mamma was removed, and the right axilla cleared of its glands and fat. The little tumour was also excised from left breast.

Description of parts removed at operation.—The right breast and neighbouring tissues with fat and glands from the axilla, weighed together 17¾ oz. An elliptical piece of skin, 7 inches long and 3 inches broad at its widest part, has been removed, and on the deep surface of the gland a few fibres of the pectoralis major muscle.

The main tumour consists of a mushroom-shaped mass, measuring rather more than 1 inch in its longest diameter. The deeper portion of it shows on section a deeply cupped surface, and has the typical appearance of a scirrhous cancer. Bands of fibrous tissue radiate from its margin into the tissues around, so as to give a puckered appearance to the involved tissues. The superficial portion of the tumour (or head of the mushroom) is softer than the other, convex on the cut surface, and of a semi-transparent appearance and pinkish-white colour. This latter portion of the tumour shows no points of degeneration; its texture is very close.

Situated immediately beneath the main tumour is another small oval tumour (three quarters of an inch in its longest diameter). It is surrounded by loose areolar tissue, and just shows upon the deep surface of the breast. It is moveable in all directions, and has all

the appearances of an adenoma. At a short distance from it is another similar but rather smaller tumour. There is very little of the mammary gland tissue remaining. The axillary glands are all small, and show extensive fatty degeneration, but no signs of new growth.

The little tumour removed from the left breast is oval (three quarters of an inch in its longest diameter), lobulated, and on section shows the usual appearance of an adenoma.

Microscopical appearances.—The main tumour has the structure of a glandular cancer. Some parts of the growth show very well the acinous type of such tumours as they occur in the breast. There are in the fibrous stroma of the tumour spaces lined with a single or at most two layers of cells, and the cells are cubical or of a low columnar form. The central spaces of these acini are empty.

In others of the stroma spaces the cell collection is for the most part solid, but there is usually at one end of the space a lumen lined with cubical or columnar cells, and the lumen itself is almost entirely filled with granular material. In yet other of the stroma spaces the cell collection is solid, as in the ordinary type of alveolar mammary cancer.

The stroma of the growth contains relatively few connective-tissue corpuscles, and there is very little small round-celled infiltration.

Both the adenomata from the right breast, and that from the left, show the usual structure of such growth, viz. that of an adeno-fibroma.

The lining epithelium of the irregular and slit-like spaces consist of, from one to several (five or six), layers of small spheroidal cells. The spaces are relatively few in number, and the fibrous tissue contains very few corpuscles. Round the spaces there are many more corpuscles, as if proliferation were occurring. There is no small round-celled infiltration. In none of the sections that were examined was there any indication of active proliferation of the lining cells of the spaces.

The patient left the hospital on the nineteenth day after the operation.

On referring to Mr. Bryant's work on diseases of the breast, I find mention made of one case in which carcinoma was associated with an adeno-fibroma of the right breast; the patient was aged forty-nine. And from the same source I learn that a specimen

of the same kind has been placed in the museum of the College of Surgeons by Mr. J. Hutchinson.

I think that the comparative rarity with which a benign, is found associated with a malignant, tumour of the breast makes the specimen worth recording, but should not feel inclined to speculate as to the origin of either tumour. *February 2nd*, 1892.

V. DISEASES, ETC., OF THE ORGANS OF MOTION.

1. *Depression on the frontal bone of a baby.* (*Card specimen.*)

By H. D. Rolleston, M.D.

There is a depressed area on the right frontal bone, $1\frac{1}{4} \times 1\frac{1}{8}$ inches, being longer from above downwards than from before backwards.

There is no fissure, fracture, or thickening of the bone. The depression is probably due to pressure exerted by the sacrum during parturition. No history could be obtained as to whether the labour was difficult or not.

From a marasmic infant aged fifteen weeks, who was in St. George's Hospital under Dr. Penrose. *January 5th*, 1892.

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2. *Congenital absence of the tibia.* (*Card specimen.*)

By J. Bland Sutton.

In September, 1891, Mr. MacLeod, House Surgeon to the Salop Infirmary, sent me a deformed leg which Mr. Rope had removed, by amputation at the knee-joint, from a strong healthy country girl, 18 years of age. The relative proportions of the legs of this girl are shown in the accompanying woodcut (see Fig. 8). It will be seen that the left leg is very short, and the foot, which is in the position of extreme talipes equino-varus, scarcely reaches to the middle of the calf of the normal leg.

The girl used a single crutch, with which she was very nimble, and used the deformed leg to advance the crutch.

The leg is remarkable from the fact that it contains no tibia, nor any fibrous representative of this bone. The fibula was short but otherwise exceedingly well developed. The bone was 22·5 cm.

FIG. 8.

Congenital absence of the tibia.

long, and presented at its proximal end an articular facet. The lower end presented its usual shape, and articulated with a broad concave facet on the astragalus. This bone was of peculiar shape and unlike any astragalus known to me, and it was firmly ankylosed

to the calcaneum. The tarsals, metatarsals, and phalanges were present in their proper order.

I made a careful dissection of the soft structures of the limb, and found all the muscles which normally arise from the tibia duly represented, and of a bright red colour. I was prepared to find the muscles normal in number, for every muscle of the leg with a tibial origin, except the flexor longus digitorum, has also a fibular attachment; this flexor was blended with the adjacent muscles, and had no separate attachment to the fibula. It was a surprise to find the muscles in such an excellent condition, but this may be explained by the fact that the nerves were healthy, and that the patient used the limb, as has already been mentioned, to advance the crutch in walking.

With regard to the muscles inserted into the tibia—the popliteus, sartorius, gracilis, semi-tendinosus, and semi-membranosus—no facts can be stated, as the soft structures at the proximal end of the specimen had been detached in cutting the flaps; and no precise statements can be made as to the relation of the parts in the neighbourhood of what should be the knee-joint.

Numerous examples of partial or complete absence of the fibula have been recorded from time to time, but I am of opinion that congenital absence of the tibia is a very rare condition.

The skeleton of the limb is preserved in the museum of the Royal College of Surgeons, London. *May 17th*, 1892.

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3. *Congenital absence of fibula, with malformation of the foot.* (*Card specimen.*)

By J. H. Targett, M.S.

History.—The limb was removed by operation from a healthy boy aged 3 years, who was born of healthy parents, between whom there was no blood relationship. The labour was normal; no instruments were used. There were three other children in the same family, all in good health and without deformity. Six months

before the birth of this child the mother fell heavily against the corner of a box, striking the lower part of the abdomen.

He walked on the lower part of the tibia, which was bent backwards and outwards, and upon the *dorsum* of the malformed foot. Hence the sole of the foot looked directly *upwards*.

Description of specimen.—The preparation consists of a right tibia, and the bones of the corresponding foot, some of which are malformed and others are wanting.

The tibia.—Upper end almost normal; shaft much flattened, so that it possesses only two surfaces (antero-external and postero-internal), and two borders (external and internal); the lowest fourth of the shaft is bent outwards and backwards to a right angle. The lower end of the bone is cartilaginous, has no malleolus, and the surface to which the foot is attached looks directly outwards and backwards. This surface is provided with two small articular facets, separated by a broad groove.

The foot consists of three tarsal, three metatarsal, and eight phalangeal bones. The tarsus bears three complete digits. Of these the innermost is the first or *great toe*, shown by the size and shape of the metatarsal bone, which bears only two phalanges, and has two sesamoid bones at its distal extremity. The tarsal bone immediately behind the great toe is undoubtedly an internal cuneiform from its shape and position; and the relation which the metatarsal bone of the middle digit holds to this internal cuneiform suggests that the middle digit is the *second toe*. The tarsal bone immediately behind the middle digit is not characteristic in shape, and may be either a middle or external cuneiform. The outermost digit is presumably the *fifth toe* from the appearance of its tarsal extremity. Of the eight phalanges there is nothing of interest to note, and it only remains to describe the third tarsal bone, by which the foot is connected with the tibia. This bone is very irregular in outline, and appears to represent the os calcis, together with the scaphoid and cuboid bones. It consists of a body and three processes—two anterior and one posterior; the latter is a conical mass of cartilage, projecting upwards among the muscles of the leg behind the lower end of the tibia. The two anterior processes are separated by a deep groove. The outer one is continued directly forwards from the body of this compound bone, and may be called the cuboid process. It articulates with the outermost metatarsal, and with the uncharacteristic cuneiform mentioned

above. The inner process is a cubical mass of cartilage, jutting out from what appears to be the sustentaculum tali. It articulates in front with both the cuneiforms, but not with the cuboid process, and presumably represents the scaphoid bone. There is nothing in the situation of the astragalus, but inasmuch as the lower end of the tibia is connected by *two* articular facets with the compound tarsal bone just described, it may be that the astragalus is represented by the enlarged inferior extremity of the tibia.

Dissection of the soft parts previous to maceration of the specimen, revealed the following abnormalities :—There was a complete absence of the fibula. The "interosseous" membrane existed, and gave origin to muscles; it was attached to the outer concave border of the tibia, and to the conical mass of cartilage projecting back from the os calcis. The muscles arising from the antero-external surface of the tibia, and also from this interosseous membrane, were—

Tibialis anticus, inserted into internal cuneiform and tarsal end of first metatarsal.

Tibialis anticus secundus, arising with the preceding from the upper four fifths of the shaft of tibia, and inserted by broad band into dorsal surface of tarsal end of first metatarsal, and by a wide expansion over the tarsus.

Extensor longus digitorum, inserted by two tendons, one by lateral expansions into second phalanx of outermost toe, the other blended with tendon of extensor proprius hallucis. There was no tendon to middle toe.

Extensor proprius hallucis. Its tendon was joined by preceding, and inserted into terminal phalanx of great toe.

There was a muscle on the dorsum of the foot, *extensor brevis digitorum*, arising by three more or less distinct bellies from the compound tarsal bone previously mentioned. It was inserted by its outermost tendon into the second and third phalanges of the middle digit, and by two other tendons into the inner and outer sides of the base of the proximal phalanx of the great toe. Arising from the concave external border of the tibia were two peroneal muscles. Of these one was attached to the whole length of this border, and was inserted into the compound tarsal bone midway between its posterior and cuboid processes; the other muscle had a smaller origin from the upper end of the bone behind the inter-

osseous membrane, and was attached to the cuboid process and the adjacent end of the metatarsal of the outermost digit.

On the back of the limb the following muscles were noted:

Tibialis posticus, arising from lower end of postero-internal surface of tibia, and inserted into scaphoid process of the compound tarsal bone.

Flexor longus digitorum, arising by two heads: one from just below the popliteus (which was practically normal), and superficial to the tibialis posticus; the other from beneath the tibialis posticus. They were joined by the flexor accessorius in the sole of the foot, and were distributed to all three digits.

Flexor longus hallucis, which did not exist as a separate muscle, but its tendon took origin from that of the flexor longus digitorum.

Soleus and *gastrocnemius*, the origins of which were damaged in the course of the amputation, but their combined tendon was traceable into the apex of the conical posterior process of the compound tarsal bone. *May 17th*, 1892.

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4. *Hereditary congenital dislocations of the radius.*

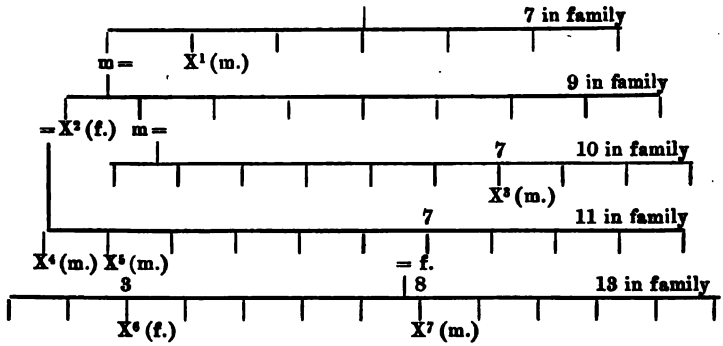
By F. C. Abbott.

Of the nine cases of congenital dislocation of the radius described in this paper, seven occurred in one family, in which this deformity has been hereditary, the cases being scattered over four generations.

Five of these cases I have personally examined and verified; in the other two I have only the statement of the relatives, that the deformity and limitation of movement was precisely the same as in those I have examined.

The relationship of these cases to one another is seen by reference to the following table:

GENEALOGICAL TABLE OF CASES.



In three of the cases only one elbow is affected, but in the other four the deformity is symmetrical, whilst in all the seven the dislocation of the radius is nearly directly forwards.

In all the cases the deformity was first noticed when the child began to use its hands, and in no member of the family was any other deformity present. We see from this table that the variation is a very persistent one, that the tendency has twice been transmitted by males, twice by females, while in only one instance has the person transmitting it been herself the subject of the deformity; and in Case 3 it has only occurred in the third generation, both father and grandfather transmitting the tendency without themselves being affected, and the affection of the grandfather's brother pointing to the deformity having existed at any rate one generation earlier still.

Description of Cases.

CASE 7.—A boy, aged 10. He died recently of enteric fever, and the elbow-joints have been dissected (*see* Fig. 9), while casts of the elbow before and after death are shown to the Society.

When examined during life the arms were symmetrical, and on both sides there was a prominence in front of the outer part of the humerus, due to the head of the radius, and the finger could be placed in the cup-shaped depression on its head. The capitellum of the humerus could not be felt, and the ulna appeared normal. Flexion and extension at the elbow-joint were free, but there was

no movement of pronation or supination, the forearm being fixed in a slightly more pronated position than the mid-position.

Abduction and rotation of the humerus allowed free pronation of the hand beyond this point, but there was no further supination, and the boy was unable by any means to turn his palms face upwards, thus causing him difficulty in holding school books, which first called my attention to the matter. There was no obvious lack of development of any muscle, or group of muscles.

CASE 6.—A girl in service. The right arm is normal, but the condition on the left side is the same as in the last case, and she complains of difficulty in holding dishes, &c., having to hold them with the left hand over instead of under them, or by resting them on the left wrist.

These are the eighth and third members of this family, and have inherited the deformity through their mother, who is the seventh member of the previous generation. She presents no abnormality herself, but the first two members of her generation are both affected.

CASE 5.—A man, aged 56. The right arm is almost exactly similar to the boy's, and on the left side the radius is also displaced forwards, but some injury to this elbow-joint in childhood obscured the exact deformity on this side. He keeps a beer-shop and does general work, finding considerable inconvenience.

CASE 4.—A man, aged 58. The arms are very muscular, and the right side presents the same deformity well marked, while on the left there is only some check to full supination, with no actual deformity.

These men have no families.

CASE 2.—An active old lady of 76. The right arm is the same as the boy's, the left quite normal. She states that she has never been able to bring the palm of her right hand to her face since birth, and finds considerable difficulty in washing herself.

The other two cases I have not personally examined, but Case 3, a lad, seventh child of the last case's eldest brother, is stated to be affected with the same deformity in both elbows;

while Case 1, the brother of the father of Case 2, also had both elbows affected.

In both these cases there are clear statements of the same limitations of movement, and consequent inconvenience.

This history does not admit of any explanation such as traumatism at the time of birth, or position *in utero;* and as the cases are so exactly similar, I think we may use the dissections of the boy's elbows as, in all probability, representing the condition to be found in the other cases.

Description of dissections (see Fig. 9).

The two elbow-joints are practically identical. Before opening the joint the radius was seen to be displaced forwards, the head lying in front of the capitellum of the humerus, with which it articulates at its back. The head of the radius is well shaped, but the neck is markedly lengthened, and bent somewhat forwards at its upper end.

The ulna, as seen from the inner side, is well formed, but from the front the coronoid process is seen to be greatly widened, coming forward as a large process on the outer side, in front of where the lesser sigmoid cavity should normally be, and projecting towards, and fused with, the neck of the radius, so as to prevent all movement between them.

The lower end of the humerus is well formed, except that the external condyle descends slightly lower than the internal, thus reversing the usual obliquity of the lower end.

Over the head of the radius a thin portion of the capsule is stretched, and this was covered by a thin layer of the supinator brevis muscle, while round its neck and altogether below the head are apparently the remains of the orbicular ligament. Otherwise the ligaments are nearly normal.

On opening the joint the capitellum of the humerus was seen to be enlarged relatively to the trochlea, and the outer margin of this latter is not so well marked as usual, owing to this enlargement of the capitellum.

The capitellum articulates in front with a concave facet on the back of the head of the radius (part of the surface that usually articulates with the orbicular ligament), and below with the upper surface of the wide coronoid process of the ulna. The humeral

fossæ are normal, except that the radial is much larger than the coronoid.

The articular surface of the coronoid process articulates with the

FIG. 9.

Left elbow-joint dissected (Case 7). a. Humerus. b. Radius. c. Ulna. d. Capitellum. e. Trochlea. f. Head of radius displaced forwards. g. Outer part of wide coronoid process. h. Extra centre of ossification between radius and ulna. (Nat. size.)

whole width of the articular surface of the humerus, the increased width of the coronoid process being altogether on the outer side,

and the outgrowth being in front of the remains of the lesser sigmoid cavity. This process is directly fused with the neck of the radius, and on cutting off some slices from it, is found to consist of cartilage and bone, bone being prolonged into it from both radius and ulna, while between the two is a distinct extra centre of ossification in the cartilage (Fig. 9, h).

No trace of a joint between the radius and ulna can be found here.

Thus the chief pathological condition found (since the lengthening of the neck of the radius and of the external condyle of the humerus are obviously secondary) is an outgrowth from the outer side of the coronoid process, articulating with the capitellum of the humerus above, fused with the neck of the radius without a joint, and pushing this forward, and possessing a separate centre for ossification.

This centre is probably that sometimes found for the coronoid process, and I think it probable that this large outgrowth is the primary fault in development; because, if it were merely secondary to the displacement of the head of the radius, I hardly think the articular cartilage would have been so smoothly prolonged along its upper surface.

That the radius was primarily in its right position is proved by the remains of the lesser sigmoid cavity.

Figs. 10 and 11 represent the dissected elbows from another case of congenital dislocation of the elbow-joints, in which a maldevelopment of the humerus is certainly the disposing cause.

These elbows were taken from a male child aged 2 months,[1] the subject of rickets, who, in addition to congenital dislocations at both elbows, was the subject of double talipes equino-varus and outward dislocation of the right patella.

During life the deformity of the elbows was so complex that the exact condition could not be ascertained. Here the deformity on the right side is not so extreme as on the left, and I think the less marked one shows well how the other has been brought about.

Description of dissections.

On the left side (*see* Fig. 10) the lower end of the humerus (a) consists only of the external condyle and capitellum (e); this

[1] Under the care of Mr. Clutton, to whom I am indebted for permission to describe the specimens.

latter is nearly globular, covered about equally front and back with articular cartilage, which is prolonged high on the inner side, where it articulates in its lower part with a new concave facet on the outer side of the head of the radius, and in its upper part with

FIG. 10.

Left elbow-joint dissected (Case 8). a. Humerus. b. Radius. c. Ulna. e. Larger articular surface, representing capitellum. f. Smaller articular surface, representing trochlea. (Nat. size.)

new-formed cartilaginous facets on the outer side of the coronoid and olecranon processes.

Lying on the inner side of the humerus, which is somewhat hollowed to receive it, and above this extension of the articular cartilage, is an irregularly shaped smooth mass of cartilage (f), ½ inch long, attached to the humerus by fibrous tissue, and articulating with the greater sigmoid cavity of the ulna, the opposed surfaces being covered with articular cartilage.

The upper end of this mass is 1⅛ inches above the lower end of the humerus, and I believe it to represent the displaced internal condyle and trochlea, for it is attached to the humerus, articulates distinctly with the greater sigmoid cavity of the ulna, and gives attachment to a considerable part of the capsule of the elbow-joint, as well as to the flexor muscles. The radius and ulna (b and c) have kept their relative positions to each other, but the two bones have been together twisted inwards, and the radius has been dislocated backwards, inwards, and upwards on the lower end of the humerus, while the ulna still continues to articulate with what

represents the trochlea, the latter having been displaced with it, and at the same time it articulates with the elongated upper part of the capitellum of the humerus by fresh facets on the outer side of the coronoid and olecranon processes.

The olecranon process has become much curved by the drag of the triceps.

The head of the radius is well formed, except that it is rendered concave on its outer side by the pressure of the capitellum, with which it articulates. The upper surface of the head is free, and points directly backwards.

The capsule is definite, and there are also orbicular fibres passing round the neck of the radius.

With regard to movements, pronation and supination are moderate, but flexion and extension very limited, and in these movements the irregular cartilaginous mass moves with the ulna.

On the right side (*see* Fig. 11) the articular end of the humerus

FIG. 11.

Right elbow-joint dissected (Case 8). a. Humerus. b. Radius. c. Ulna. e. Capitellum. f. Cartilaginous mass representing internal condyle and trochlea. g. Olecranon. (Nat. size.)

is deeply cleft by a groove, extending round from front to back of the articular cartilage, thus dividing it into a larger outer and a smaller inner part, each subglobular in shape, and representing the capitellum and trochlea respectively. This groove also exists above, and thus nearly, but not altogether, as on the opposite side, separates trochlea and internal condyle from the rest of the bone.

The two humeral condyles appear normally developed.

The forearm bones keep their relative position to each other, and are both dislocated directly backwards on the humerus.

The head of the radius is very well formed, and its cup-shaped upper surface points directly backwards, below and behind the humerus. It articulates by a new concave facet on the front of the head with the under part of the capitellum of the humerus, and this capitellum also articulates (as on the left side) with new facets on the outer side of the coronoid and olecranon processes.

The ulna, although displaced backwards, still articulates by the whole length of the olecranon with the inner articular surface of the humerus, this being rendered possible by the great bending of the olecranon, which is more marked than on the opposite side. It also articulates with the outer articular surface of the humerus by two new-formed facets on the outer side of the coronoid and olecranon processes, and with the radius by the lesser sigmoid cavity as usual.

With regard to movements, flexion and extension take place through about 50°, and there is considerable pronation and supination.

The condition on this side is thus a less marked degree of what is met with on the other; for had the cleft in the articular end of the humerus proceeded farther, so as to separate the inner part completely from the remainder, and had this been carried up half an inch, with the ulna still articulating with it, we should have had precisely the same condition as is met with on the opposite side.

I know of nothing in the development of the humerus, or in comparative anatomy, that will account for this cleft condition of the lower end of the humerus, and which in this case is the primary cause of the deformity.

The last case is that of a girl aged 21,[1] shown this evening. She is the eldest of a family of eight, and the only one affected, and the deformity was first noticed at 2 to 3 months of age.

The right elbow is normal, but on the left side there is a congenital dislocation of the radius backwards and outwards.

The head of the radius is easily felt behind, thickened, and the hollow in the head somewhat obliterated.

[1] Under the care of Mr. Lawford, to whom I am indebted for permission to show the case.

The humerus is normal, but the ulna on this side is one inch shorter than on the other, and there is some wasting of muscles on this side.

Flexion is free, but extension cannot be carried quite to a straight line. Pronation is perfect, but supination is stopped at slightly beyond the mid position. She has experienced no difficulty except that she cannot lift heavy weights with this arm.

Among all the cases of congenital dislocation of radius that have been previously described, I have only been able to find one in which the deformity was hereditary.[1]

This patient was a woman with backward dislocation of the head of the left radius; she was one of a family of eleven, eight of whom presented various abnormalities of joints, and one brother had an exactly similar dislocation of radius; while the father had similar deformities, and stated that they existed in his father, father's brother, and father's brother's children.

In the case of the family described in this paper no other deformity is known, all the members being particularly strong and well made except in this one particular.

Also in the great majority of recorded cases, dissected or otherwise, the prime cause has appeared to be non-development or deficient development of the capitellum of the humerus; but in both these pairs of dissected elbow-joints it is well formed, larger than normal, and certainly not at fault. *April 5th*, 1892.

Bibliography.

Adams.—'Todd's Encyclop.,' Part 9, p. 75.
Allen, William.—'Glasgow Med. Journ.,' 1880, xiv, 44—50.
Cruveilhier.—'Path. Anat.,' Pls. iii and iv.
Dupuytren.—'Journ. Hebdom. de Méd.,' vii, 45.
Froriep.—'Chir.,' Copper Pl., Tab. cccl, figs. 1—6.
Guérin.—'Gaz. Méd. de Paris,' 1841–2, ix, 97—145.
Hellis.—'Lancet,' 1886, ii, 249.
Humphry.—'Med.-Chir. Trans.,' vol. xlv.
Malgaigne.—'Rev. Méd. Chir. de Paris,' 1853, xiii, 216—227.
Phillips, Sydney.—'Brit. Med. Journ.,' 1883, i, 773.
Pye-Smith.—'Lancet,' 1883, i, 993.

[1] Dr. Pye-Smith, Sheffield Med.-Chir. Soc., 'Lancet,' February, 1883, p. 993.

Sandifort.—'Mus. Anatomy,' Tab. ciii, fig. 3.

Smith, R. W.—'Dublin Journ. M. Sc.,' 1850, x, 213—216; 1850, xiii, 208—210.

Symington.—'Journ. Anat. and Phys.,' 1877-8, xii, 445—447.

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5. *Charcot's disease of the hip.* (*Card specimen.*)

By J. Jackson Clarke, M.B.

The capsule of the joint and surrounding bursæ are distended. The head and neck of the femur have been absorbed. There are loose bodies in the joint, and dislocation by deformation. From a man of 50, with symptoms of tabes for fifteen years, and of disease of the hip for five years. *November 27th*, 1891.

VI. DISEASES, ETC., OF THE ORGANS OF SPECIAL SENSE.

1. *Hereditary melanotic sarcoma of the choroid.*

By A. Quarry Silcock, M.D.

The specimen of choroidal sarcoma shown, affected the left eye of Elizabeth G—, aged 20, married and pregnant, who was admitted into the Moorfields Eye Hospital in October, 1890, in order that I might remove the globe.

When the eyeball was excised the optic nerve was found to be infiltrated by the neoplasm, and was dealt with accordingly.

The following is the report of Mr. Treacher Collins, F.R.C.S., Curator of the Hospital, on the eye:—"Growing from the lower half of the choroid of the left eye is a deeply pigmented tumour, which extends from the ciliary processes to beyond the upper margin of the optic disc. It fills rather more than half the vitreous. The growth appears to have started in the outer part of the choroid, and is a mixed spindle- and round-celled sarcoma; pigment is distributed through it in the form of circular masses and scattered granules."

This patient's mother had her left eye removed at the Moorfields Hospital twenty years previously, and the specimen was preserved in the museum. Reference to the Curator's Report of the time ('Royal London Ophthalmic Hospital Reports,' vol. vii) shows that the mother's eye became affected, and ultimately blind, whilst pregnant with her sixth child, and that it was excised twelve months after the birth of the seventh child, Elizabeth G—, whose case I have just described.

It will be noticed that the sarcoma in the mother's case affects the same part of the choroid as in the child's. Mr. Collins informs me that the growths are practically identical histologically.

The family history of the mother is also remarkable, as I learn

from the above authority,[1] that "one of the patient's sisters died at the age of forty years of tumours of the breast, which 'went all over her' and formed a lot of hard lumps. The same sister lost one of her eyes a short time before her death; it became blind spontaneously and shrunk up. A twin sister of the mother lost an eye after confinement; it shrunk and became smaller than the other. The mother's father lost an eye by inflammation; it had not been injured, and shrunk up."

Remarks.—That a neoplasm of a similar kind and affecting a similar organ should occur both in parent and child is not very unusual, perhaps; but the close resemblance of the growth in all points, and the fact that the mother was the subject thereof at the time she was pregnant with the child in whom a like condition was ultimately developed (and in the same eye as that of the mother), are interesting features in the history of malignant neoplasms.

The eyes lost by members of the mother's family were probably destroyed by other than neoplastic influences, but so strange a series of coincidences almost suggests an hereditary vulnerability of the tissues of the eyeball. *May 17th*, 1892.

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2. *Hæmatoma auris.*

By E. T. Wynne, M.B.

The specimens exhibited are two ears with hæmatoma, preserved in spirit, and a series of sections from several specimens obtained from lunatics. For comparison a section from a normal adult ear and from a patient aged seventy are shown—the latter as an example of senile degeneration.

The cartilage of the normal ear is seen to be a uniform plate of fibro-cartilage bounded by a fibrous sheath—the perichondrium. The senile ear shows various changes. To the naked eye it looks patchy, and at these places the microscope shows the cartilage being replaced by fibrous tissue, or a loose tissue composed of stellate cells, or undergoing a hyaline transformation, the plump cartilage-cells being represented by a few nuclei.

[1] Op. cit.

Here and there the perichondrium is seen to send processes of fibrous tissue into the cartilage, and these processes contain vessels. It is, I believe, the rupture of these vessels that gives rise to the "insane ear," the characteristic feature of which is the permanent distortion produced by the hæmorrhage.

If the sections of hæmatoma are examined, similar degenerative changes are found in the cartilage. The cartilage shows a great tendency to split, especially where the matrix has assumed a hyaline character.

The hæmorrhage in the specimens is seen to be not only beneath the perichondrium, but also in the cartilage itself, which in some of the specimens is much broken up.

In the majority of cases the cartilage is split into two portions, the fissure running obliquely from one perichondrial surface to the other. The fragments are displaced by the effusion of blood. The clot formed becomes more or less organised, and the fragments thus become fixed and the permanent distortion results.

The hæmorrhage seems to start from new vessels in the processes of the perichondrium mentioned above, which often completely traverse the thickness of the cartilage. Making its way along the new-formed tissue, the blood reaches the perichondrium on either side. It then spreads beneath the perichondrium, displacing the divided cartilage in its progress. If it comes in contact with a part rendered exceptionally friable by degeneration, it breaks up the cartilage at that spot.

In the formation of hæmatoma auris, hæmorrhage of course also occurs into the loose subcutaneous tissue, and traces may sometimes be found in the form of pigment. This part of the hæmatoma is, however, readily absorbed, and *post mortem* the above condition only is seen, if the patient does not die soon after the formation of the hæmatoma.

The latest description of this lesion is by Dr. Tishkoff.[1] He states that "the characteristic form of the hæmatoma is caused by the cavity between the cartilage and perichondrium." This cavity he attributes to rupture of new-formed vessels, which produce absorption of the cartilage. The initial process he ascribes to an inflammation of the perichondrium; but whether he means by this changes such as are seen in senile degeneration of the cartilage, or more acute inflammation immediately preceding the formation of

[1] 'Lancet,' Feb. 13th, 1892, p. 381.

the hæmatoma, does not appear from the abstract in the 'Lancet.'

From the specimens exhibited I think it is clear that the changes predisposing to "insane ear" are similar to those of senile degeneration, and that the characteristic appearance of the lesion is due to fracture and permanent displacement of the cartilage.

I wish to express my indebtedness to Dr. Wiglesworth, Medical Superintendent of the Rainhill Asylum, for much of the material with which I have worked. *May 3rd*, 1892.

VII. DISEASES, ETC., OF THE DUCTLESS GLANDS.

1. *Case of malignant disease of the thyroid gland involving the œsophagus and cervical vertebræ, with a deposit of thyroid tissue in the bone.*

By Edgar Willett.

This case occurred in St. Bartholomew's Hospital, and was under the care of Mr. Thomas Smith, who kindly gave permission for its publication. The patient was Mrs. B—, a widow aged 48, who gave the following history:

In December, 1889, she first complained of pain in the back of the neck, and this gradually increased.

In June, 1890, she noticed a swelling on the right side and in the front part of her neck. It was quite painless. It continued to enlarge, and was soon followed by a similar swelling on the left side of the neck.

In July, 1890, from increasing weakness she took to her bed, and was admitted to the hospital on October 1st. Her personal history was good, and there was no history of tumours in her family. She then had in the front of her neck an irregular swelling. It was hard, ill defined from its deep situation, mostly on the left side, fixed, not tender; the skin was not adherent, and no fluctuation could be detected at any point. There was doubtful movement of the tumour with the larynx on deglutition. She still had considerable pain, but at the back of the neck. A consultation was held, and the general opinion was that she had caries of the cervical vertebræ, with an independent enlargement of the thyroid.

She remained in the hospital, and her head was fixed both by sandbags and, later, by a poroplastic collar, which gave her some relief.

On March 13th she first complained of dysphagia.

On March 20 she was not so well, being troubled with a cough, and her temperature was now of a hectic character. She gradually sank, and died on March 29, 1891, one year and three months after the onset of symptoms.

The specimens shown consist of (*a*) the larynx and thyroid gland and surrounding parts, and (*b*) a portion of the cervical vertebræ. There is a large rounded swelling involving the left lobe and isthmus; it is slightly nodular on the surface, and is firmly adherent to the left common carotid, jugular vein, and neighbouring structures. The œsophagus has been laid open from behind, and shows a large, ragged, ulcerated surface, apparently formed by direct extension of the disease. The trachea is somewhat flattened, and is pushed over towards the right. The bodies of the fourth and fifth cervical vertebræ, which have been sawn through longitudinally, are occupied by a deposit of fine spongy appearance. When examined under the microscope after softening, this deposit showed true thyroid structure lying in and partly replacing the substance of the bone.

November 3rd, 1891.

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2. *Substernal goitre.* (*Card specimen.*)

By J. H. Targett, M.S.

The specimen exhibited, which was presented to the College of Surgeons by Dr C. Gross, was removed from the body of a woman aged 68, an artificial flower maker, who died in an infirmary. She had been under observation for three years previously, suffering from slight dementia of a senile character, but was able to be up and about the wards most of the day, and required no particular treatment. One morning she was found dead in bed.

Autopsy.—The lungs were emphysematous but otherwise healthy. The pericardium contained about four ounces of serous fluid. The heart was moderately hypertrophied, weighing fourteen ounces, and its valves were healthy. Liver and spleen normal. Kidneys small and hard.

Between the lungs was a large tumour, consisting of two lobes joined together by connective tissue. Of these the larger lobe was

about the size of a cocoa-nut, and was situated on the right side of the mediastinum; while the smaller was to the left, and in size equalled that of an orange. Both lobes were loosely attached to the front of the trachea by connective tissue.

Description of specimen.—The specimen exhibited is the larger portion of the tumour. It measures five inches in length and four inches at its widest part. Its external surface is marked by large rounded projections and intervening grooves, as if it had been moulded by the adjacent structures. The substance of the tumour is so hard that a saw was required to divide it. The section reveals many smooth-walled cysts scattered throughout the tumour, the largest being an inch and a half in diameter; and the intervening tissue is in many parts infiltrated with calcareous material.

Histologically the tumour resembles a goitre. It has an abundant fibrous stroma, in which follicles of various sizes are embedded. These follicles are chiefly filled with epithelial cells, but in some parts the central cells have broken down into a granular material, in which cholesterin plates may be seen. In other places, though few in number, small masses of colloid substance are met with, surrounded by a single layer of cubical epithelium, as in normal thyroid tissue. The stroma is permeated by many large vessels, and in some sections there are appearances of old hæmorrhages together with organised blood-clot.

December 15th, 1891.

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3. *Fibrous atrophy of the right adrenal (? tubercular); left adrenal large.* (*Card specimen.*)

By F. Charlewood Turner, M.D.

In vol. xxxiv of the Society's 'Transactions' (p. 436) there is a description by Dr. Hadden of fibrous atrophy, or cirrhosis, of the adrenals in a case of Addison's disease, with a drawing showing fibrous thickening and nucleated connective tissue growth in the zona glomerulosa, which was the region principally affected.

The organs now exhibited present a unilateral lesion, affecting especially the medullary tissue, and associated with renal cirrhosis

and the cardio-vascular lesions of chronic Bright's disease; though the presence of a minute cretaceous nodule in the affected organ, and of the cretaceous residuum of a bronchial gland, suggest the possibility of a tubercular origin of the lesion in this case also.

The *left* adrenal is of an unusually large size, and apparently quite normal in structure. It measured, after prolonged preservation in spirit, 2½ inches by 1, and weighed 76 grains.

The right adrenal was less than one third of the left, diminished in all its dimensions, and altered in shape. It measures, allowing for portions removed, about 1½ by ¾ inches, and weighed about 24 grains, making similar allowances. It is flattened, apparently by the drawing in of the projecting fold on its anterior surface, to the body of the organ, and consequent disappearance of the normal fissure in its lower border and hilum. The upper and lower borders were both convex, owing to contraction of both ends, and especially of the posterior end.

The preparation shows the two ends and the central part of this organ, between which portions have been removed. They are separated from one another to exhibit the cut surfaces of the fragments.

The fibrosis is most advanced in the central portion, which was with difficulty pierced by the small pins by which it is fixed; and the section of its narrower, or posterior, border presents little appearance of adrenal tissue. In the section of its anterior and broader end the knife encountered a minute cretaceous nodule in the fibrous tissue.

The cut surfaces of the ends of the organ show, at their lower borders, defined and encapsulated narrow tracts of apparently normal adrenal tissue. These are of circular section, and separated by a tract of fibrous tissue from the rest of the organ, which is seen to be the seat of a destructive lesion.

In the cut surface of the smaller (posterior) end of the organ, from the neighbourhood of which the section shown under the microscope was taken, the pale cortical zone is marked off by a narrow horseshoe-shaped band of pigmentation, from an unpigmented central area. Examination of the corresponding areas in the microscopical section shows that there has been a development, in the centre of the medullary tissue, of a profusely nucleated connective-tissue growth of indefinite character, which

surrounds the central vessels, including small groups of adrenal cells, and appears to have pushed out the cortex, with disruption of its continuity in places by extension of the growth to the surface; and the narrow band of pigment is seen to be due to a yellowish-brown pigmentation of cells in the deepest part of the cortex, interrupted at points where the continuity of that zone has been broken by the outward extension of the central growth. The stroma of the cortex appears thickened, and at one part especially there is a notable fibrous thickening of the stroma of the medullary tissue.

The section of the apparently healthy lower border of the organ shows comparatively little structural change under the microscope. There is a very notable thickening of the stroma of the cortex at one part, which has only half the depth of that at the opposite side. In the outermost zone tracts of nucleated fibrous tissue extend inwards from the greatly thickened fibrous capsule.

The investing capsule is greatly thickened throughout by compact fibrous tissue with many small nuclei. The arteries are conspicuously thickened. The veins are congested, and there are recent extravasations around some of them.

This section seems to indicate the active stages of the lesion by which the organ has been contracted up and deformed, and which would appear to have invaded it from the hilum, to have completely destroyed its central part, and to have left only its lower borders comparatively intact.

At the anterior end of the organ two tracts of apparently normal adrenal tissue are seen at the lower border of the section. They are both of circular section and surrounded by thickened capsules, and are one above the other. It seems possible that the upper one may represent the border of the projecting fold of the organ, drawn up by cicatricial contraction of its central part.

The section shows also, what is observable in sections from healthy organs, a high degree of fatty degeneration and swelling of the cells of the outer part only of the zona fasciculata, the inner boundary of the change extending in a pretty regular line round the central part; those cells of the columns crossed by this line, which fall within it, having a cloudy protoplasm with a varying tinge of pigmentation. This seems to indicate that the conspicuously pigmented line separating the opaque outer zone of the transverse section of the normal adrenal from the (normally)

equally colourless, but more translucent medullary part, is not a part of the latter, but corresponds to the deeper part of the cortex, the pigmentation of which is not obscured by fatty degeneration or infiltration, and swelling, which account for the opacity and pallor of the outer part of it.

The organs were obtained from the body of a woman, aged 49, who was admitted into the London Hospital with cirrhosis of the kidneys and hypertrophied left ventricle, with high arterial tension, attended by attacks of severe præcordial pain. Her kidneys were granular and contracted, weighing only 4 oz. The heart weighed 11 oz. There was a cretaceous nodule at the root of one lung, but no signs of tuberculosis. There was a fibro-myoma of the size of a hazel nut in the right ovary.

The most notable features about the lesion of the supra-renal body in this case are—

1. Its unilateral nature, and its association with an abnormal development of the unaffected organ.

2. The destruction, in part complete in part incomplete, of the greatest part of the organ, with contraction and deformity, by a cirrhotic lesion, which has left a portion of it practically intact.

3. The association of this lesion with cirrhosis of the kidneys, and with the cardio-vascular changes of chronic Bright's disease.

If the large size of the unaffected left adrenal may be compared with the compensatory overgrowth of one kidney observed when the functional capacity of the other has been wholly, or in great part lost, its presence would indicate that the function of the adrenal is one which is essential to the organism, and one not adequately performed by other organs—under the conditions here present, at all events.

The facts of the case, as far as they go, accord with the results of the analytic researches of McMunn, and with the observed anatomical association of *totally* destructive lesions of these organs with the clinical symptoms of Addison's disease, in indicating the existing of such an essential and proper adrenal function.

As regards one fact that is considered to be incompatible with the existence of such a function—the absence of the symptoms of Addison's disease in cases of malignant disease of these organs—it may be pointed out that in no case of malignant disease of these organs can any proof of total, or even very extensive, *destruction* of

the adrenal cells be adduced; nor any evidence that the modification in the growth of the adrenal cells, incidental to their becoming affected with malignant disease, is incompatible with the continuation of their proper vital function. The channel of removal of the products of that function being lymphatics or blood-vessels, no interference with any such functions can arise, as in the case of glandular organs with excreting ducts, from a physical impediment to the escape of such products.

In the later stages of fatal malignant disease, with much anæmia and low percentage of red corpuscles in the blood, a defect, or even loss, of organs having the function of assisting in the removal of the colouring matter of the blood from the system, might not have any marked result in the accumulation of pigment in the skin.

April 5th, 1892.

VIII. DISEASES, ETC., OF THE SKIN.

1. *A large sebaceous horn, removed from a woman aged* 56. (*Card specimen.*)

By Wm. F. Haslam.

It was situated on the scalp, behind the coronal suture and just to the right of the middle line. The patient noticed it first six

Fig. 12.

Sebaceous horn of scalp.

years ago as a "small lump," no doubt a distended sebaceous gland. There does not appear to have been at any time any in-

flammation of the sac, or appreciable amount of discharge as from a breaking down of its wall; but this "small lump" gradually increased in size, and, from after a time being covered with a scab, gradually acquired its present characters (*see* Fig. 12). Its dimensions were as follows:—Length along curves, 8¼ inches; greatest circumference, 2⅛ inches; circumference at growing point, 1⅝ inches; and near the end, 2 inches; weight, 430 grains. Its surface, of a light brown colour and in places rather waxy in appearance, is marked by longitudinal lines and furrows, and on its upper surface about an inch from the end there is a deep transverse crack. In consistence it is very hard, and gives out a clear note on being struck, its general appearance being that of a small ram's horn. It seems to be a good example of the so-called sebaceous horn, arising in connection with a distended gland that gradually discharged its contents on the surface, where drying, they became converted into a horny material.

It was not the cause of any pain, and only a trifling inconvenience, as it was easily hidden by a high cap. Its base was evidently in the skin, and it could to some extent be moved at its attachment. Removal was easily effected by a circular incision and a few touches at the base with a scalpel.

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2. *Guinea-worm embedded for twenty-eight years under the skin of the calf of the leg.* (*Card specimen.*)

By H. D. Rolleston, M.D.

The specimen consists of a calcified rod, about 6 inches long, which lies in the subcutaneous tissue over the gastrocnemius. It lies in the long axis of the leg, and at each end becomes coiled up, forming a flat plate.

The unravelled part is as large as, or a little bigger than, an ordinary vas deferens. Where the unravelled part joins the two coiled-up parts the continuity of the worm is broken for a short distance.

From a soldier, aged 50 years, who died in St. George's Hospital,

He had been fourteen years in India, where twenty-eight years before his death he was in hospital for over 100 days with a guinea-worm in his right leg. As he was getting rid of this, another developed in his left leg, which, owing to the treatment adopted, did not work its way out, but remained *in situ*.

The patient himself gave the above details. *May 3rd*, 1892.

IX. MORBID GROWTHS.

1. *Enchondroma following upon hereditary multiple exostoses.*

By Joseph Griffiths, M.A., M.D.

The specimens I exhibit are the bones of the left lower limb, which was amputated about the middle of the thigh. On the lower half of the femur there are seven exostoses, two large and pedunculated, the others small and sessile; the largest arises by a broad thick pedicle from the antero-internal surface of the shaft 3 inches above the lower end, and takes a direction upwards, inwards, and forwards for nearly 2 inches, where it suddenly bends outwards, upwards, and forwards at an angle with the first portion of about 120°, and continues for nearly 3 inches before it ends in an expanded and nodulated extremity which overlaps the anterior surface of the bone; each nodule is covered by a thin layer of hyaline cartilage, and the whole of the cartilage-tipped surface is enveloped in a bursal bag which contained fluid resembling synovia. The next largest is one of remarkable shape, closely resembling an Indian club, and it arises by a narrow pedicle from the upper end of the inner terminal line of the *linea aspera* on much the same level as the former, is directed upwards and inwards, and ends in a slightly expanded, flattened, and nodulated extremity; in this also each nodule is tipped with hyaline cartilages, and the whole was surrounded by a bursal bag. Two other smaller sessile exostoses arise from the same line near the adductor tubercle, and two others of much the same size as the last, one from the upper and the other from the lower end of the outer terminal line of the *linea aspera;* and another on the anterior surface of the shaft immediately above the trochlea, besides numerous small nodulations in the region of the epiphysial line. The part of the shaft immediately above the articular end is flattened from before backwards, but not otherwise changed.

On the upper end of the shaft of the tibia is a large rounded and slightly lobulated mass consisting of hyaline cartilage, and measuring 6 inches in the vertical and 4 inches in the transverse diameter. It arises from the outer surface, and extends chiefly towards and on the posterior so as to surround nearly three fourths of the circumference of the bone; in its growth it has more or less completely enveloped the upper end of the shaft of the fibula. The mass replaces the periosteum, and has encroached upon the outer layers of the dense bone of the shaft, causing its partial absorption. In structure it is like an ordinary enchondroma of the bones; that is, it consists of rods of cartilage, which are separated from one another by a variable quantity of fibrous connective tissue, in which the blood and lymph vessels traverse. The central portion of this great mass had undergone liquefaction into a thick glairy yellow and transparent fluid like thick synovia, owing to fatty and other forms of degeneration; in other places the cartilage rods had become calcified, and, it may be worthy of note, the calcification was found in some instances affecting only a narrow rim at the periphery of the rod. Just where the fibula emerges from this mass there is a small exostosis from the posterior surface of the shaft. The lower ends of both bones are much enlarged and synostosed for nearly 3 inches, and on the posterior surface of the synostosed shafts there are nodular thickenings. The bones of the foot are free from bony outgrowths with the exception of the metacarpal bones, which at either extremity show many nodulations.

The specimens were removed in December last from a man aged 31 years, healthy-looking, rather short, but strongly built, slight knock-knee of left limb, dark hair and blue eyes, and deeply marked by smallpox. He has had some lumps on his bones ever since he can remember, and all, with the exception of the cartilage mass on the left tibia, have grown more or less in proportion to the growth of the body, and have for some years remained of the same size; the cartilage mass began to increase about a year ago, and has since grown more rapidly, causing him pain and much inconvenience from its bulk. There are many exostoses on the right lower limb, in much the same situation as those found in the left, namely, the lower end of the femur, upper and lower ends of both tibia and fibula; but there are no distinct lumps on the bones of the upper limbs, nor on those of the trunk, and the only change that

can be detected in them is thickening and nodulation at the epiphysial lines of the upper ends of the humeri, lower ends of radii, inner ends of clavicles, and along the free border of the spine of the left scapula.

He has one brother who, like himself in complexion and build, suffers from similar lumps and a deformed arm; another brother and two sisters, who take after their mother who is not affected by any lumps, are said to be quite free from any such lumps. The father, 63 years, silk weaver, after whom the son who is the subject of this paper takes, is short, strongly built, has dark hair and blue eyes, and suffers from exostotic lumps in the lower limbs near the lower ends of the femora, upper and lower ends of the tibiæ and fibulæ, and a lump in the left loin, attached either to a lumbar vertebra or to the hinder part of the ilium, and a small exostosis on the dorsum of the first phalanx of the left index finger. His paternal grandfather, who resided in London, had similar lumps on his bones, one of which, situated in the right loin, grew to a large size, and for which he was admitted into St. Bartholomew's Hospital, where he soon died at the age of sixty years. A paternal aunt suffers from similar lumps, and, like the brother, has a deformed arm.

Similar cases of multiple exostoses have been reported since Barwell, Lloyd, and Stanley drew attention to them in this country, and a few instances may be found in the 'Transactions' of the Society; but the more interesting communications on the subject are those by O. Weber in 'Virch. Arch.,' Bd. xxxv, in which he points out the hereditary feature, and illustrates a case of multiple exostoses associated with enchondroma of the pelvis, which gave rise to secondary growths in the lungs, thus causing death.

Again, Bessel Hagen, in 'Langenbeck's Arch.,' vol. xli, p. 444, draws attention to these cases, and refers especially to the deformities of the bones that are commonly associated with the affection, and he considers the growths to arise from a condition of the bones allied to rickets. I do not propose to enter this evening upon the great question of the ætiology of these growths and the probable bearing it may have on the origin of other tumours, and shall therefore content myself with saying that some are satisfied with the Cohnheim theory, and others look upon them as the products of morbid disturbances during the growth and development of the bones.

February 2nd, 1892.

2. *Congenital myxo-sarcoma of the neck, containing striped muscle-cells.* (*Card specimen.*)

By J. H. Targett, M.S.

Description of specimen.—This tumour (R. C. S. Museum, No. 416 C) was removed by operation from the neck of an infant. It is roughly pyriform in shape, and measures 2 inches in diameter at the larger end. The exterior is much lobulated, and bundles of muscular fibres are blended with its tough fibrous capsule. The cut surface shows that it is composed of large alveolar spaces filled with a soft gelatinous substance. In the recent state this was of a greyish-red colour, and mucoid fluid freely oozed from it. Histologically the tumour consists of a delicate stroma permeated with capillary vessels, and infiltrated with cells of many sizes. The most striking of these cells are about four times the size of a red blood-corpuscle; they stain deeply with logwood, and possess two, three, or more nuclei. In sections that have been embedded in celloidin they have a rounded outline, and appear succulent, not to say bloated. Mingled with these are many small round, angular, and tailed cells, such as are met with in sarcomata; but no distinctly epithelial elements have been discovered in the examination of many microscopic sections. Where the cells are less numerous the delicate spongy stroma comes into view, and the section there resembles a myxoma, or myxo-sarcoma.

In lightly stained sections a few of the long-tailed cells, which have the appearance of the spindle-cells in some sarcomata, when examined under a high power may be shown to be transversely striated, like voluntary muscle-cells. These striped cells are long but narrow; some are collected or felted together in small bundles; many are mixed irregularly with the round cells of the growth.

Congenital sarcomata containing striped muscle-cells have been met with in various parts of the body, notably the kidney. (For references see Cristiani, 'Journal de l'Anatomie et de la Physiologie,' Paris, 1891.)

History.—The patient, aged 6 months, was admitted to a hospital with a swelling on the left side of the neck, which had

existed from birth. This swelling had grown with the child until the last five weeks, during which time it had more rapidly enlarged. A fortnight before admission it was tapped, but only mucoid fluid and blood came away.

On admission there was a swelling of oblong shape behind the left sterno-mastoid muscle, about the size of a large hen's egg, extending from just below and behind the ear to the clavicle. It was soft, elastic, semi-fluctuating, but not translucent; it appeared to be moveable over the deeper structures, and caused no interference with respiration or deglutition. At the operation the tumour was found to be deeply placed beneath the sterno-mastoid, near the transverse processes of the cervical vertebræ. After some difficulty the whole tumour was dissected out, with the exception of a pedicle which seemed to run downwards and backwards in the direction of the scapula. The wound healed rapidly, but a swelling still existed at the lower part of the neck just above the clavicle. This swelling, which was no doubt the end of the pedicle above alluded to, steadily enlarged, and was therefore removed one month after the first operation. It was found to extend well below the clavicle. The child was in excellent health six months after the second operation; there was no sign of recurrence.

May 3rd, 1892.

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3. *Tumour of the thigh in Scarpa's triangle lasting nine years (sarcoma ?).*

By John R. Lunn.

Annie D—, aged 16, was admitted into St. Marylebone Infirmary March 3rd, 1888, in a very anæmic condition, apparently due to hæmorrhage from a pulsating, ulcerating, conical swelling in front of the right thigh, about the size of a cocoa-nut. The friends stated that she had lost two quarts of blood before admission.

Five years ago, or nine from the present time, her right big toe nail was avulsed at the West London Hospital. Afterwards she noticed a swelling in the right groin. (On inquiry being made

at the West London Hospital no record of the case could be found.)

In November, 1883, she was admitted into the Children's Hospital, Paddington Green, under the care of Mr. Watson Cheyne, to whom I am indebted for the following notes. Annie D—, aged 11, was admitted November 16th, 1883, with swelling in the right thigh. The tumour was first noticed two years before, and slowly increased in size, but not so much lately; the child was well nourished and in good health.

On admission a firm elastic tumour was seen in Scarpa's triangle, bounded above by Poupart's ligament; the femoral artery was pushed to the outer side and felt pulsating there. It is of the size of an orange, smooth in outline, not adherent to the skin, not moveable over the foramen; no enlarged glands and no large vessels on it or in the neighbourhood.

On November 20th, 1883, an incision was made over the tumour; it was firmly adherent by a broad base to the periosteum of ilium, very vascular, not adherent to the neighbouring parts, enveloped in a capsule. The diagnosis was a sarcoma of the periosteum of ilium, and the attempt to remove it was given up. After the operation Mr. Cheyne states the patient developed an irregular temperature without any evident reason about the wound, and he thought secondary deposits were occurring, and some irregular nodules were to be felt in the abdominal walls. The parents took the child out.

When the girl was admitted under my care in March, 1888, the tumour was then the size of a cocoa-nut, fungating and pulsating, situated in Scarpa's triangle.

It appeared firmly attached behind, tender on pressure; well-marked pulsation on the outer side of the swelling was noticed, over which could be heard a loud bruit. A bruit could also be heard over the cardiac area and all the large vessels. On pressure over the common femoral artery the pulsation was not completely stopped, nor the bruit, but only altered in character.

The right iliac artery was weaker than the left. The patient during her sojourn remained in the same condition, with an irregular temperature varying from 98·6° to 103·8° F.

She had several attacks of severe hæmorrhage, which were easily stopped by pressure over the oozing surface. An exploratory operation was suggested, but the friends would not consent to

have anything done, and they took the child home in April, 1888.

She was readmitted on December 18th, 1888 (and had then come out from the Cancer Hospital, where electrolysis had been tried) in about the same state, with some slight extension of the growth inwards towards the adductor muscles, and with some suspicious nodules in the abdominal walls above the pubes.

She was transferred to her own parish, Kensington, in January, 1890, under the care of my friend Mr. Potter, who kindly gave me permission to publish the case, and to whom I am indebted for one of the photographs and final history of the case.

Mr. Potter, assisted by Mr. Keetley and others, removed a portion of the growth by placing an elastic tourniquet round the base of the tumour; the vessels were tied with catgut, and there was little bleeding, but the girl died from exhaustion in four days. No *post-mortem* was allowed by the friends.

Dr. Bristowe saw the case with me when under my charge, and examined the murmurs over the heart and large blood-vessels, and referred me to a somewhat similar case of his published in the 'Lancet' of May 9th, 1885, in which there were pulsating tumours with murmurs occupying the infra-spinous fossa of the right scapula, and two swellings on the buttocks, over which were well-marked murmurs. Dr. Bristowe told me he thought the murmurs were due to the condition of the vessels of the tumours, and to the arteries, not the veins. No cardiac disease was found at the *post-mortem* on this case.

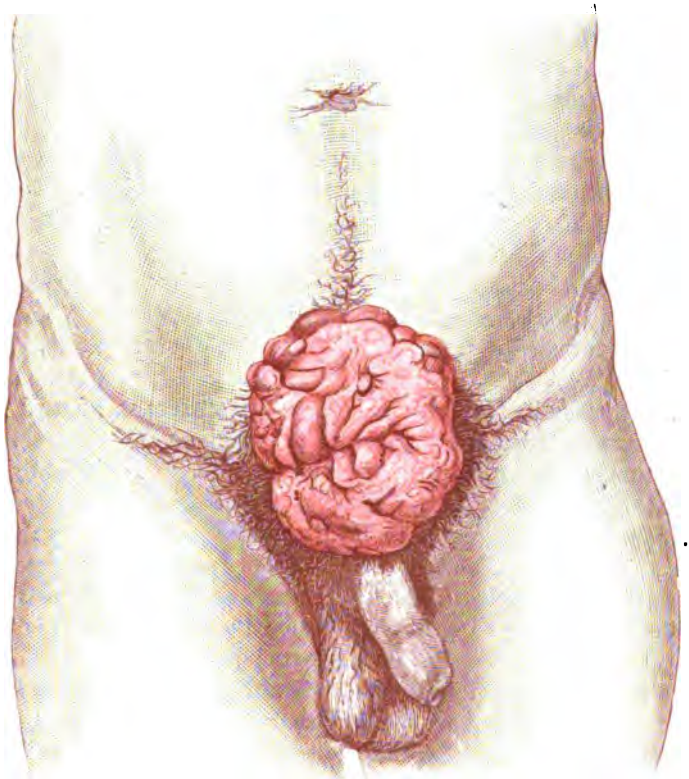
The chief interest of this case appears to be its long duration lasting nine years, and its slow increase in size. The growth was firm and elastic at its onset, and I cannot help thinking that it was fibrous and venous in its origin, and then had taken on a sarcomatous growth (spindle-cell sarcoma), as the specimen shows under the microscope. *May 17th*, 1892.

4. *An unusual form of wart (plexiform sarcoma—Billroth). (Card specimen.)*

By J. Bland Sutton.

J. P—, aged 36 years, was placed under my care by Dr. J. J. Clarke for a large tumour growing from the skin immediately above the pubes. The tumour (see Fig. 13) consisted of a short but broad stalk surmounted by a mass as large as a closed fist; its surface was as red as a cock's-comb, soft, smeared over with purulent

Fig. 13.



An unusual form of wart.

fluid, and gave forth a most offensive odour. The glands in each groin were enlarged, and the patient complained of pain in the left half of the thorax and severe cough. He stated that he had had for many years a small wart among the pubic hair; two years ago this began to grow, and gradually assumed its present size and disgusting condition. The fluid discharged from the mass was so free as to saturate his clothes each day.

The patient thought the growth to be venereal in nature, and for many months he had, with much ill-directed industry, anointed it freely with saliva; this mode of treatment he believed was most efficacious for syphilitic lesions.

The tumour was such that I had never seen before, and the emaciated condition of the man, his enlarged glands, and thoracic trouble, were so strongly suggestive of general infection that prudence dictated non-interference, but the condition of the patient was so pitiable that humanity urged the removal of the stinking mass. This was readily accomplished by a few sweeps of the scalpel. The wound healed kindly and well, and the inguinal glands dwindled and resumed their natural size, but the cough persisted, and the temperature varied from 100° to 103°. Eventually Dr. J. K. Fowler took charge of the patient, and he was transferred to a medical ward.

The thoracic signs still continued obscure, but the mystery was solved six weeks later, for the patient died suddenly, and the autopsy revealed a large aneurysm of the thoracic aorta, which had ruptured.

The tumour was fairly firm, but the cut surface was dotted with numerous yellow masses of about the size of peas. The stalk of the tumour was of a more fibrous texture. Histologically the tumour consisted of very large columns of epithelial cells; these columns were so large as to be distinctly visible to the eye in the stained sections. The cells in these columns were very large, and possessed oval nuclei. Each column was limited peripherally by a delicate layer of young fibrous tissue; the centre of many of the columns contained a yellow elongated patch of necrotic tissue. The rounded ends of these columns with the yellow streak in the centre, the regular disposition of the cells, and the limiting outer membrane formed an appearance very like an enormous bulb of a developing hair. The framework of this tumour consisted of firm fibrous tissue.

On looking up the literature of the subject with the view of classifying this tumour, I found that Mr. McCarthy published in the 'Transactions,' vol. xxxi, p. 256, a similar case which grew from a wart on the cheek of an old man. The account of this case is illustrated by some admirable drawings, and I find that the histological features agree with those presented by my case. Mr. McCarthy identifies the tumour as the plexiform sarcoma of Billroth, and certainly the crude sketch furnished in Billroth's work serves as a means of identifying these tumours, for their structure is very peculiar, and it is interesting to note that Billroth was much perplexed by this kind of tumour; so was McCarthy; it is therefore needless to add that I suffered in the same way.

McCarthy, in the very careful account of his case, writes, "It requires a large degree of faith to believe that these cord-like masses are of connective-tissue origin;" and he concludes thus:—"The appearance of the individual cells suggests rather some form of rapidly growing epithelial structure." So convinced is McCarthy of the non-sarcomatous nature of this kind of tumour that in the 'Supplementary Reports,' vol. xxxiii, he writes, "Repeated microscopic examination has, however, convinced me that the plexiform cord-like bands are composed of epithelial cells, and the growth appears to have been a very large and unusual form of wart." (Mr. McCarthy informs me that his patient died in 1889, nine years after the operation, and never had the slightest recurrence.)

It seems to me that this is the proper view to take of these tumours. They are certainly very rare, and, so far as we know at present, they look more formidable than they really are, for there is no evidence to lead us to believe that they are malignant. These cases should be recorded so as to make surgeons more familiar with a condition which up to the present time has been a clinical puzzle, and is certainly a pathological curiosity.

May 17th, 1892.

5. *Epithelioma involving naso-pharynx, nasal fossæ, air-sinuses, orbits, brain, &c., of eleven years' duration.*

By A. Quarry Silcock.

Charles T—, aged 15, was admitted to the Moorfields Eye Hospital in August, 1882. He had applied some months previously as out-patient for relief, by reason of a smooth, hard, ill-defined swelling over the left frontal bone, just above the inner half of the left eyebrow. The swelling had been noticed twenty months. It subsequently increased in size, was evidently connected with the frontal bone, and was diagnosed a sarcoma thereof. Soon the left eye became proptosed, he began to complain of great frontal headache, and six weeks before the date of admission he had a "fit" of an epileptoid character, followed by unconsciousness; ultimately the fits occurred more and more frequently.

The following note was made in the Moorfields Hospital Register on his being admitted for the first time:—"General smooth, large prominence of the left frontal bone, with no outlying nodules about it. Left eye pushed down and out; upper and inner part of left orbit filled with growth. Left nostril plugged by growth. Left optic neuritis. V. = $\frac{20}{20}$."

Since that date the growth increased in extent in all directions, until the head assumed the remarkable characters seen in the specimen. He died last year, quite unconscious; but from what I could learn he appears to have been capable of understanding what was said to him (though very deaf) up to a comparatively short time before he succumbed.

The following report on the specimen has been kindly made for me by Mr. J. J. Clarke, F.R.C.S., Curator and Pathologist, St. Mary's Hospital:

"The growth involves the naso-pharynx, nasal fossæ, air-sinuses, orbits, brain, &c. The face presents in the left orbital region a prominence as large as a man's fist, due to an exuberant growth pushing forward and infiltrating the eyeball and the skin. The latter is nodular at one part. The section shows that the base of

the skull and the frontal bone are increased to an average thickness of two inches. Attached to the bones is a mass of growth, which fills the naso-pharynx and the nasal cavity, and projects beneath the skin of the forehead on the one hand, and on the other extends into the anterior fossa of the cranial cavity as a spongy mass, which invades and infiltrates the frontal lobe of the left hemisphere. The remainder of the brain is displaced, and has caused expansion and thinning of the bones forming the skull-cap. The part of the brain infiltrated by the growth presents the sponge-like appearance of alveolar tissue.

Microscopy.—A portion of the soft growth from the naso-pharynx at the base of the skull was first examined. It presented irregular groups of epithelial cells surrounded by abundant fibrous supporting tissue. The general appearance was that of an ordinary squamous epithelioma. Several cell-nests were found in this part of the growth, but elsewhere they were absent. The characters of other parts of the growth were similar to those of that at the base of the skull. Thus, the prominent warty growth around the left eye was epitheliomatous save at the surface, which was papillomatous, there being a distinct interval between the advancing epithelioma and the hypertrophied skin. Neither on the face nor in the pharynx had ulceration taken place. The whole of the thickened base of the skull consists of epithelioma tissue, which is ossified to a considerable extent. The affected part of the brain was not microscoped, but its macroscopic characters are unmistakably those of alveolar growth, and there is little doubt that it is part of the epitheliomatous neoplasm."

Remarks.—The case is interesting, not only as showing the length of time a being can exist under such unfavorable circumstances when more or less carefully tended, but also in respect of the exact nature of the growth. I should be very glad to hear any suggestions as to the primary seat of the neoplasm. Did it arise in one of the frontal or ethmoid sinuses, as its epithelial characters might suggest? *May 17th*, 1892.

6. *A case of cancer, cirrhosis, and tubercle; unusual distribution of secondary cancer.*

By P. H. Pye-Smith, M.D., F.R.S.

A man, aged 58, was brought into Guy's Hospital under my care in March, 1892. From his appearance it was supposed that he was intemperate, and this was afterwards confirmed; but no other history was obtainable. He had led a vagabond life, and seemed to have taken little but gin for some time before his death. The liver was much enlarged, there was no ascites or jaundice, no enlarged lymph-glands, and no anasarca. The mouth was full of blood when he was first seen, but there was no other evidence of hæmatemesis, and no vomiting then or afterwards. He was delirious, and never recovered his senses. Icterus came on in a day or two and continued till death, which happened by coma on the 15th of March.

The diagnosis during life lay between cirrhosis and cancer of the liver, and I decided in favour of the former, partly from the apparent absence of pain, partly from there being no evidence of disease of the stomach, rectum, or other usual seats of primary cancer; and this conclusion was confirmed by the mental symptoms and the mode of death.

At the autopsy the liver was found much enlarged, weighing 9 lbs. It was covered with small uniform granulations, and on section was fatty, tough, and uniformly indurated, without the islets of hepatic tissue or the "hobnails" on the surface, which mark the more common type of gin-drinker's liver. Microscopical sections showed large tracts of fibrous tissue irregularly disposed, and enclosing groups of lobules of nearly equal size. The lobular structure was in some places perfect, in others destroyed; the secreting cells were full of oil, but in a state of fatty repletion, not degeneration. The fibrous tissue contained numerous leucocytes, showing a comparatively recent interstitial hepatitis. In the anterior border of the right lobe was a large umbilicated cancerous nodule. The spleen was swollen and the organs deeply jaundiced. So far the view taken during life was confirmed.

In the stomach, however, was found a malignant ulcer an inch in diameter, round, with greatly swollen and infiltrated edges; it occupied the posterior wall close to the lesser curvature, and nearer the cardiac than the pyloric orifice. A large mass of cancerous lymph-glands lay behind the stomach, and the pancreas was infiltrated by a similar growth, which did not touch its duct or cause obstruction to that of the liver.

A nodule of secondary cancer was found in one adrenal and another in the thyroid body, and nowhere else. On section both the primary gastric growths and the secondary tumours in the pancreas and elsewhere were found to consist of the ordinary glandiform, epithelial type, rather firm in texture.

The lungs, which were free from cancer, showed the fibrous cicatrix of old phthisis at both apices, and also several small groups of recent tubercles with surrounding inflammation in one of the upper lobes. No tubercle was found elsewhere, but the phthisical process, which had been checked for a time, was evidently again making progress.

Lastly, there was a patch of grey hepatisation in the right lung (middle lobe) which had passed into a state of gangrene. No trace of foreign material could be found there, so that it did not appear to have been caused by particles of food entering the air-passages.

Remarks.—1. The anatomical characters of the liver corresponded to Charcot's account of hypertrophic cirrhosis, and the presence of jaundice and absence of ascites agreed with his account, but there was no doubt of the alcoholic origin of the disease, and the spleen was enlarged. Moreover, as Dr. Price, of Reading, has shown, gin-drinkers' livers are quite as often above as below the normal weight.[1] The smaller and more contracted the liver the greater the pressure on the portal capillaries and the earlier will ascites supervene. But there is, I think, no reason to believe that there are two different kinds of chronic interstitial hepatitis, different in origin and pathology, and with constant difference of symptoms.

2. The coincidence of cancer and cirrhosis in the liver is of course a mere accident; the former process was certainly subsequent to the latter, and there can be no reason why the infection of cancer, whether it be particulate or chemical, should not infect

[1] 'Guy's Hospital Reports,' vol. xlii, p. 295.

a cirrhotic liver as well as a healthy one. Still the fact that secondary cancer reproduces the exact histological characters of the primary growth seems to show that it is not the result of a modifying influence upon the cells of the organ, but an immigration of germs from the original seat of disease.

3. The coincidence of cancer and tubercle in the same patient is not so rare as was once supposed. I have myself met with it more than once before. Cases like the present seem to show that there is no natural incompatibility in the two processes, for both were going on at the time of death. The reason why we seldom find them together is that they belong for the most part to different periods of life. A person affected with tubercle commonly dies of his disease before he attains the age favorable to the development of cancer, or the tubercle becomes obsolete. It is only when, as in this case, an ancient physical process which had become quiescent is renewed after a long interval, that there is much chance of a more rapidly fatal disease interposing and cutting short the belated tuberculosis.

4. Latency of gastric carcinoma is not infrequent. I have seen it in a case of colloid cancer of large extent; but it is difficult to explain why, in these exceptional cases, all the usual symptoms are absent.

5. What led me to bring this case before the Society was that it shows, as I believe, a rare and exceptional distribution of secondary cancer. The deposits in the thyroid and adrenal are neither of them common, but the large mass of infiltrating cancer in the pancreas is, as a secondary growth, extremely rare. I have only met with one or two other cases, whereas the pancreas or its duct is very often the seat of primary carcinoma.

May we not lay it down as a pathological rule that secondary cancer is rare in organs which are the frequent seat of the primary disease; and *vice versâ*, that primary cancer is seldom found in organs which are most frequently affected by secondary deposits?

The breast and cervix uteri in women, the testis in man, the stomach and rectum in both sexes, the lip, tongue, and œsophagus —the favourite seats of primary carcinoma—as well as the pancreas, penis, prostate, and bladder, and the skin, where it also is frequently met with, are certainly very seldom affected by secondary cancerous nodules. The occurrence of a malignant growth in both mammæ is perhaps not an exception, but analogous

to the appearance of the disease in one breast after the other has been removed.

On the other hand, the liver, the lungs, and the lymph-glands, which are the most frequent seats of numerous secondary cancerous nodules, are very seldom attacked by primary cancer; the liver only as a rare exception, the lungs still more rarely, and the lymph-glands perhaps never.

The bones probably come next as seats of secondary deposits, and true cancer is scarcely ever known to begin in them. The kidneys are occasionally the seat of primary and not infrequently of secondary carcinoma. The spleen is only as a rare exception affected by cancer at all, and this is also true of the brain.

Sarcoma with a different primary distribution has, if I may use the expression, a different rule of multiplication. It often affects several places at once, and its favourite seats—the bones, the eye, the skin, the ovary, the kidneys, the lymph-glands—are some of them provided with epithelium, though connective tissues are believed to be its original seat. It is certainly more often met with in the lymph-glands as a primary than as a secondary growth, but on the whole there is not the distinction between its original and subsequent localities which is remarked above with respect to true carcinoma.

If the law in question holds generally true (and, like other laws, it may sometimes be broken without ceasing to be a law) it furnishes, I think, an argument in favour of the opinion that cancer is not the result of any general disposition, diathesis, or dyscrasia; while (as Waldeyer taught us) it only begins in epithelial structures, and begins in only one structure at a time. The secondary growths are, for the more part, in non-epithelial structures, *their* place being determined not at all by the histology of the organ, but by the readiness with which it can be infected from the single primary seat of the disease. The route thence is most commonly by the lymphatics, but also by the veins. Thus cancer of the submaxillary glands follows that of the tongue, of the axillary that of the breast, and of the lumbar that of the testis; while the liver is most often infected by secondary cancer from the stomach or rectum or pancreas, and the lungs from other organs.

In its secondary distribution cancer more resembles syphilis, and sarcoma more resembles pyæmia. *April 5th*, 1892.

7. *Pathological conditions of the mamma associated with carcinoma.*

By Raymond Johnson, M.B., B.S.

[With Plate V.]

A point of primary importance in the surgical treatment of carcinoma of the breast is, whether it is necessary in all cases suitable for operation to remove the whole breast. These investigations were undertaken four years ago at the suggestion of Mr. Marcus Beck, with the object of ascertaining whether pathological evidence can be obtained which may be of service in answering this question. I must at the outset express my great obligation to the Surgical Staff of University College Hospital for their great kindness in allowing me free use of their cases.

My object has been to investigate the condition of the glandular tissue in breasts the seat of carcinomatous growths. This has been done by means of careful naked-eye examination of all parts of the organ, as well as by means of microscopic sections.

From a practical and clinical point of view the most useful division of carcinoma of the breast is into two varieties—the nodular and the diffuse. The diffused variety admits of two possible explanations. Thus we may suppose the growth to arise at one spot, and to spread widely through the lymphatic channels; or it may be that a more or less wide-spread tendency to carcinomatous change affects the whole gland. Both these processes occur. A specimen is shown, taken from the left breast of a woman aged twenty-seven years, the whole of which, with the exception of the upper and inner quadrant, was infiltrated with rapidly growing carcinoma. The section is taken from the apparently unaffected part, and we clearly see masses of cancer-cells lying in spaces in the stroma between the acini, which are themselves apparently healthy. These spaces are probably lymphatics.

As an example of what I believe to be the other form of diffusion, a specimen is shown from a breast the seat of a small slow-growing colloid cancer. The remainder of the gland had become enlarged

and hardened during the few months before the patient came under observation. A section shows it to be infiltrated with carcinoma. The smaller ducts remain in an apparently healthy condition, and around them are grouped small solid masses of large epithelial cells, an appearance unmistakably suggesting to my mind that a wide-spread change has affected the epithelium of the acini, with consequent development of the infiltrating variety of carcinoma. It is probable that the unusual cases, in which more than one carcinomatous growth is present in the same breast, may, in different instances, be examples of both the above-mentioned processes.

It is, however, with the nodular form of carcinoma that we are now chiefly concerned, and it is to the condition of the breast in such cases that my attention has been more especially directed.

Allow me to refer to the case of a woman, aged thirty-four years, under the care of Mr. Godlee. At the extreme axillary border of the left breast was a carcinomatous growth scarcely larger than a hazel-nut. If it be ever advisable to remove the tumour and leave the breast, one can imagine no more favorable case than this for the partial operation. The whole gland was, however, excised, and at the sternal border were two minute nodules, which under the microscope proved to be typical carcinoma. Further sections were made from the centre of the breast, which to the naked eye seemed healthy, and the acini are seen to be transformed into large spaces more or less completely blocked by proliferated epithelium. When last seen, thirteen months after the operation, the patient was free from recurrence.

Since our attention was drawn to the subject by Heidenhain I have examined in all cases the fascia on the pectoral surface of the gland, and have several times found there the minute nodules of growth which he has described. A section of such a nodule is shown in which the growth is seen to be invading the surface of the pectoral muscle. Such nodules can only be found on the closest examination, and must obviously escape detection in the examination of the breast before removal.

As another example of the conditions which may be detected with the naked eye, may be mentioned the presence of cysts. I am doubtful whether small cysts are more common in carcinomatous breasts, than in those of women free from carcinoma, but of the age at which it is most common.

I have no evidence showing more than an accidental connection

between the two conditions. It is not unlikely that ducts may be blocked by the growth, and may thus become cystic and the seat of intra-cystic growth. A drawing is shown of a small cyst, the lumen of which is completely surrounded by a ring of small papillomata. With the connection between such cystic changes and the development of duct carcinoma we are not now concerned.

In the large majority of cases, however, the naked eye fails to detect any obvious pathological conditions.

A drawing is exhibited showing the appearances of a microscopic section in such a case. Scattered widely throughout the gland are columns of cancer cells lying apparently in lymph-spaces. The glandular elements appear to be normal. Although from a clinical point of view this case obviously belongs to the nodular variety of carcinoma, the microscope showed it to be in reality an infiltrating form. I have only met with this solitary example of such a condition.

It is, however, to a condition of epithelial proliferation that I would especially refer. This is by no means uncommon, and in the best marked examples one finds the acini somewhat enlarged, and the lining epithelium proliferating so as to form a thick layer, or to completely block the lumen of the acinus. The individual cells also present marked alteration in appearance. They are large, the nucleus being surrounded by a considerable amount of protoplasm; they stain less deeply with logwood, and the outline is often ill-defined. In fact, they much more closely resemble cancer cells than the cells of normal acini. The condition which I am describing is well shown in a specimen exhibited. In the centre of the breast of a married woman aged forty was a small ill-defined induration. Being doubtful as to its nature Mr. Godlee incised it, exposing a cut surface looking like normal breast tissue, but feeling harder than natural. The small piece was excised, and the microscope shows in it the appearances above described. The changes here seen are probably inflammatory, and to such a condition one might apply the name chronic proliferative mastitis. It requires no flight of imagination to suppose such a condition developing into carcinoma. The patient remains free from recurrence fifteen months after the operation. Similar changes were found in the breast of a patient whose opposite breast had been excised several years previously for carcinoma. The breast under consideration was excised by Mr. Berkeley Hill on account of slight

DESCRIPTION OF PLATE V.

Illustrating Mr. Raymond Johnson's paper on Carcinoma of the Mamma. (Page 170.)

From drawings by the author.

FIG. 1.—Section of breast tissue taken from a part of the organ distant from a small nodular carcinoma. *a*, duct; *b*, acini; *c c*, columns of cancer-cells lying apparently in dilated lymphatic spaces.

FIG. 2.—Proliferative changes in epithelium of breast in a part of the gland distant from a small peripheral carcinoma. (Zeiss obj. D.)

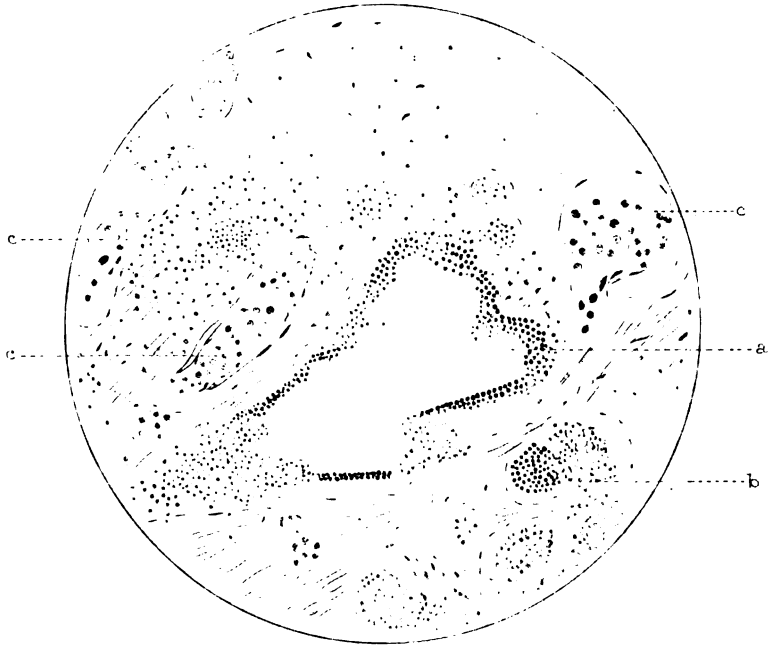


Fig. 1.

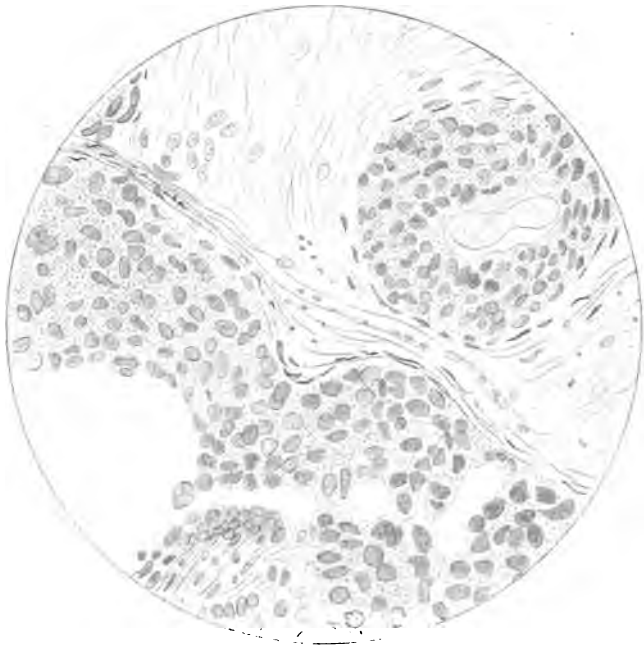


Fig. 2

R. Johnson del

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eczema of the nipple, and an indurated condition of the gland tissue. In the case of the tongue we have a chronic inflammatory condition—chronic superficial glossitis—frequently appearing as an antecedent of carcinoma; and I would venture to suggest that these proliferative epithelial changes in the mamma may stand in the same relation to the development of carcinoma in that organ. There are numerous points of interest in connection with such changes on which at present I have not sufficient evidence to allow me to speak. Such points are their relation to antecedent acute inflammatory conditions, whether they are unusually common in the breasts of women in whom the inherited tendency to carcinoma is strongly marked, and whether they are at all commonly present in chronic lobular mastitis. I am at the present time investigating the changes met with in the atrophying breasts of old women (in conjunction with my friend Mr. C. D. Cooper, Assistant Medical Officer to St. Pancras Infirmary), but so far have not found changes so marked as in some of the carcinomatous breasts examined.

I would arrange the conditions which may be met with in the carcinomatous breast as follows:—(*a*) Gland tissue to all appearances healthy. (*b*) Gland tissue atrophied, with large admixture of fat and fibrous tissue. (*c*) Chronic proliferative epithelial changes. (*d*) Infection of the gland through the lymphatics. (*e*) Cystic changes. (*f*) Presence of simple tumours. (A card specimen is shown to-night by Mr. White, Surgical Registrar to University College Hospital, of a breast containing a carcinoma and two adenomata.)[1]

The conclusion to which the above observations seem to point is that in many cases of carcinoma of the breast of the nodular variety there is a wide-spread tendency to disease throughout the whole organ. The practical indication from these considerations alone is that in all cases of carcinoma the aim of the surgeon should be as thoroughly as possible to remove every part of the organ. I am aware that we must put against this the experience of so high an authority as Mr. Butlin, who says, "I do not know when the complete removal of the mamma became a necessity, for I have not been able to lay my hand on the earliest proposals for it. Nor do I know the exact grounds on which it was in the first instance recommended. But I have no doubt it was the result of *a priori* reasoning, and was founded on the impression that the

[1] See above, p. 120.

whole of the mammary gland is in an unhealthy state, and so predisposed to cancer that the disease will almost assuredly occur in any portion of it which is left behind." Further, speaking of the subject of recurrence Mr. Butlin says, "Certainly in the vast majority of instances there is nothing to lead one to believe that the new growth arises in the outlying lobules of the mammary gland, or in any remains of the parenchyma of the gland."

I have had very few opportunities of following up cases in which a partial excision has been performed. I have, however, been able to trace five cases in which this practice was followed, the tumour in all of them being removed with a broad margin of the surrounding tissue. It so happens that in all recurrence took place in the remainder of the gland. In two cases in which the tumour was a colloid, the disease recurred in the breast without showing the colloid change. In one case after a partial operation the patient was seen about four years later, with the whole of the remains of the breast infiltrated with hard growth and firmly fixed to the ribs.

In the operation of excision of the breast there are three ways in which fragments of the gland are apt to be left: (1) at the periphery, particularly in cases where the breast tissue spreads widely, especially towards the axilla; (2) on the surface of the pectoral muscle; and (3) beneath the skin in reflecting flaps from the surface of the gland, for at those points where the breast is held to the skin by the fibrous bands known as the suspensory ligaments of Sir Astley Cooper, the breast tissue comes very close to the surface.

It thus seems to me probable that one will be doing the best for the patient in removing as freely as possible the skin overlying the breast, and in carefully and thoroughly cleaning the surface of the pectoralis major. The importance of the latter precaution, even though the tumour itself be not adherent to the muscle, is shown by a consideration of the nodule invading the muscle above described.

With regard to the free removal of skin, only experience can show whether the increased freedom from recurrence is sufficient to justify, as a line of practice, the method described by Mr. Watson Cheyne in the 'Lancet' of this year, viz. the complete removal of the skin and the partial filling up of the gap by skin grafting.

Microscopic evidence can be brought forward that this escape of small fragments of breast tissue in the ordinary operation of ex-

cision does occur. A specimen is shown of a small nodule of keloid excised from the scar twelve months after excision of the breast by Mr. Marcus Beck. The nodule was suspected to be a recurrent growth. It consists of dense fibrous tissue, beneath which are numerous acini of the gland, which must have been divided in reflecting the skin from its surface.

In a small recurrent nodule of carcinoma invading the surface of the pectoral muscle remains of gland tissue are seen, suggesting that the recurrence had origin in a fragment left behind in turning the breast from the surface of the muscle. Similarly, I have several specimens of small recurrent growths in which remains of gland tissue are clearly seen in microscopic sections.

The evidence seems sufficient to suggest that remains of breast tissue form at least one starting-point of recurrent growths, and the condition of the gland tissue in cases of carcinoma gives strong support to such a view, for it is highly probable that any fragments of the gland left behind may be the seat of one or other of the changes above described. Recurrences of such an origin one would expect to be situated around the scar, and beneath rather than in the skin.

In conclusion, I would impress upon the members of the Society that the practical object of this communication is to show that in carcinoma of the breast there is strong pathological support to the practice of the thorough removal of the gland, as far as practicable, in all cases. *January 5th*, 1892.

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8. *On some histological changes in the breast found in association with glandular carcinoma.*

By Cecil F. Beadles, introduced by Victor Horsley, B.S., F.R.S.

[With Plates VI, VII, VIII.]

Introduction.—Much has been written regarding the histology of glandular carcinoma of the mammary gland, but it appears that the breast apart from the actual growth has received very little of this attention, and certainly not as much as it would seem

to deserve. That inflammatory and atrophic conditions of the gland acini are changes frequently present in the immediate neighbourhood of the advancing neoplasm is well known; but if breasts that have been amputated for malignant growths are carefully examined, we may, I believe, discover, at a distance from the tumour, conditions of the breast tissue which are not only extremely interesting in themselves, but such as may be of the greatest practical importance in explaining in many cases the mode of recurrence of the disease after its removal, and also that of the origin of the so-called primary growth.

History.—Although I have made search in the literature of cancer of the breast, I have not found more than the following allusions to the subject of the present communication:

Cornil ('Du Cancer et de ses Caractères anatomiques,' Paris, 1866) says that mammary cancer very often begins by an excessive production and hypertrophy of cells in the lobules and glandular ducts, and goes on to say that "it is by studying the knots or little secondary tumours, which follow the growth of a mammary scirrhus, that we learn the mode of origin of cancer in these tissues."

Creighton ('Report of the Medical Officer of the Privy Council and Local Government Board, 1875') has, amongst other conditions, described in the case of a mammary tumour of the bitch, a proliferation of the epithelial cells in the acini of the rest of the breast.

During my term of office as House Surgeon to the Cancer Hospital, Brompton, my attention was early directed to the condition of the breast tissue external to carcinomatous tumours, and especially to certain small nodules which I found at a considerable distance from the primary growth, and particularly in the neighbourhood of the pectoral fascia. To elucidate the true nature of these changes it was necessary of course to examine the tissue microscopically, and the following are the methods employed.

Material and methods.—In all, I have examined nearly 100 breasts, each of which was the seat of a primary carcinomatous growth, *i. e.* true alveolar carcinoma, whether scirrhous or encephaloid. In every case the organ was within an hour after removal placed in Müller's fluid for about a week, and then the hardening was completed in alcohol. The sections were cut with the freezing microtome in gum, and stained with the ordinary watery solution of logwood, clarified, and mounted in balsam.

Conditions found.—Breasts in which carcinomatous tumours occur, are never in what may be called a normal state. It must first be premised that there are certain changes in breasts of all women who have ceased to bear children, and have reached the age at which scirrhus usually shows itself, and which therefore should be regarded as merely atrophic. Unfortunately these retrogressive changes in the human breast due to age, &c., are not yet sufficiently defined and determined with certainty, to enable one to assert confidently that the appearances about to be described bear a definite relation to the carcinoma they accompany, and are not signs of ordinary degradation.

I shall, therefore, simply proceed to describe systematically the changes which I have observed in the breasts examined, and which, as already stated, were the seat of a primary carcinomatous growth.

The extreme rarity of more than one palpable primary malignant tumour in the breast is well known, the only exception being what eventually turns out to be a soft, rapidly growing encephaloid, which, in its earliest stage, may appear as several separate nodules, coalescing before they have reached any noteworthy size. It is easy, therefore, to observe the occurrence of anything like distant or peripheral nodules in the substance of the gland should such exist. As a matter of fact, if a breast be examined immediately after removal and before being placed in any form of hardening medium, it is often possible to make out with the finger small hard nodules situated at a distance from the tumour, and having no apparent connection with it. These vary in size from a centimetre in diameter down to a small pea or less, the latter being the more frequent. A lymphatic gland frequently found lying upon the pectoral fascia, beneath and to the outer side of the breast, is not to be mistaken for one of these nodules; and in passing it may be mentioned that this gland often escapes infection when the axillary glands are extensively diseased. Sometimes, however, nothing more than a slight thickening can be felt in some parts of the breast. If one of the nodules be removed, and after hardening in Müller's fluid sections stained with logwood be examined microscopically, it will invariably be found to contain undoubted foci of carcinoma. These foci are often seen to be divided by bands of fibrous stroma into roundish areas of equal size, varying in number according to the size of the nodule, and often less than

half a dozen. This character is sometimes preserved to a slight extent in the large primary tumour. Usually these nodules are surrounded by a small-celled infiltration which shuts them off from the neighbouring gland acini. These acini are sometimes quite normal in appearance, but more often they exhibit certain well-marked changes, to be described further on. Even when no distinct nodule can be made out, but only the slight thickening of the gland tissue referred to above, the centres of such thickening may contain minute but genuine cancer nodules. More often, however, there is nothing which one can say positively is cancerous structure, but at the same time the tissue is certainly not that of the normal breast.

Before proceeding further as to the nature of the change here referred to, it will be better to mention briefly some of the conditions that may be observed with more or less frequency in all breasts containing carcinoma, but not necessarily presenting nodules or thickenings. These changes are fairly numerous, and occur in the stroma and also in the parenchyma of the organ, one or other of these or both together being affected. They are, in short, what are usually described under the term chronic interstitial mastitis, with others more properly of an adenoid character. We see the former in its earliest stage where there is a small round-celled infiltration of the connective tissue surrounding the acini with but little or no change in the epithelium, although there may be a slight increase in the number of cells within the cavities. The small round cells may spread beyond the immediate neighbourhood of the acini into the surrounding areolar tissue. It is, of course, usual to find a small round-celled infiltration at the edge of an advancing carcinoma; of this, however, we are not now speaking, but of what may be seen elsewhere in the breast, *i. e.* away from the actual tumour.

The larger ducts sometimes contain in their walls a localised collection of small round cells, with no noticeable changes in the epithelial lining. These aggregations of cells may of course be not necessarily pathological.

Again, we may find that the natural areolar structure of the breast is replaced by a denser fibrous tissue; this may be associated with a shrinking of the alveoli, degeneration of the epithelium, and its disappearance, and may be a more or less general condition present throughout the whole breast. The denser connective

tissue which normally encapsules the lobules is sometimes greatly thickened, presenting a homogeneous appearance; and when this is very marked, and limited to a group of lobules, we have what is practically a minute fibroma. With this change in the stroma is associated the production of cysts, varying in size from little above the normal diameter of ducts to such as are visible to the naked eye. These cysts may be lined with a single layer of healthy glandular epithelium, or by several; in the latter case they are more massed in places. The lumen often contains some degenerated cells with retained secretion; occasionally, however, the whole cavity is filled with a colloid mass, and no lining epithelium can be made out. Some of these may possibly be serous cysts arising in connection with lymphatics. This cystic condition may be found affecting the whole breast; it is probably little owing to the tumour, although the condition may be increased from the tumour exerting pressure on neighbouring parts, and occluding ducts. In addition to the formation of cysts we generally notice that in some of the alveoli there is a marked proliferation of the epithelium, the acini being much enlarged, and the lumen entirely filled with cells of a uniform shape and size, each containing a round nucleus (Plate VII, fig. 1). When the acini, thus distended with epithelial cell-masses, have reached four to five times the normal size, the central cells in part degenerate and break down, only imperfectly staining with logwood.

Returning again to the stroma, it may be mentioned that that immediately surrounding the acini is sometimes formed of a connective tissue younger than normal, being apparently composed almost solely of fibroblasts varying much in character, and presenting an embryonic appearance indistinguishable from sarcomatous tissue. An interesting form of alteration in the fibroid stroma occasionally observed is that in which connective-tissue cells with their elongated nuclei run parallel around the acinus, and having between them rows of what appear to be small uniform cells with round nuclei,—the same structure so frequently seen forming the stroma of some rapidly growing scirrhous tumours. The presence of this form of stroma is not common, and appears almost invariably to be associated with changes in the epithelium within the acini now to be described.

If we now examine a series of sections from the thickenings, *i.e.* not nodules, in outlying parts of the breast already referred to

we shall probably see, with a low power of the microscope, what at first sight appears to be nothing more than a condition somewhat resembling adenoma (Plate VI). There are round or oval masses of cells arranged in groups, each group being surrounded by a distinct capsule, and separated widely from one another. The stroma may take the character of any one of those previously mentioned, but more often it is the seat of a simple round-celled infiltration, with some increase of the connective-tissue nuclei. The cell-masses vary in size from that of normal acini to many times their diameter; when exceptionally large the breast tumour with which they were associated was usually of an encephaloid nature. If we now use a higher power, it will be seen that the epithelial cells vary much in size, the central being for the most part larger, with sometimes a distinct row of small cells externally (Plate VII, figs. 2 and 3). When the growth is of the hard scirrhous form, the cells found under these conditions are generally of two distinct types: the one cell is small, almost filled by a round darkly staining nucleus, and is indistinguishable from normal glandular epithelium; the other large and irregular, with a faintly staining oval nucleus, often not in the centre of the cells, having, in fact, all the characters of a malignant cell. Between these two kinds of cells all intervening stages exist. In cases of soft glandular cancer the larger nuclei are generally of rounder form, differing little from the smaller nuclei except in size. Although the whole cell-masses may be composed of non-degenerate epithelium, yet this is not usual; in the majority of cases the central part is occupied by a granular or amorphous mass, which does not take the logwood stain, and in this mass some remnants of nuclei of small size may be detected only faintly coloured, undoubtedly degenerated epithelial cells, and accompanied with what seems to be altered secretion. The degenerated cells are often of a yellowish-brown colour, and we may also find groups of oil globules that have apparently taken up a yellow tinge from the bichromate solution. Many cell-masses are elongated into columns, often connected together by narrow bands of cells of similar character, some exhibiting rounded bulbous ends which are about the size of normal acini. These bulbous ends present at their margins, except where the communication exists, the smaller epithelial cells described above as peripherally situated in the acinus, and have either a distinct lumen or the centre is occupied by cells of various size and form. The

DESCRIPTION OF PLATE VI.

Illustrating Mr. Cecil F. Beadles's communication on some Histological Changes in the Breast found in association with Glandular Carcinoma. (Page 175.)

From drawings by the author.

Section of breast tissue bordering on a small hard nodule situated at a considerable distance from the tumour, which was of three months' duration. The tumour proved microscopically to be a typical scirrhus. (Zeiss obj. A A.)

S C. One of the roundish areas into which the nodule was divided. There are irregular large cell masses, surrounded by a small-celled infiltration.

S C'. An outlying group of irregular cell masses.

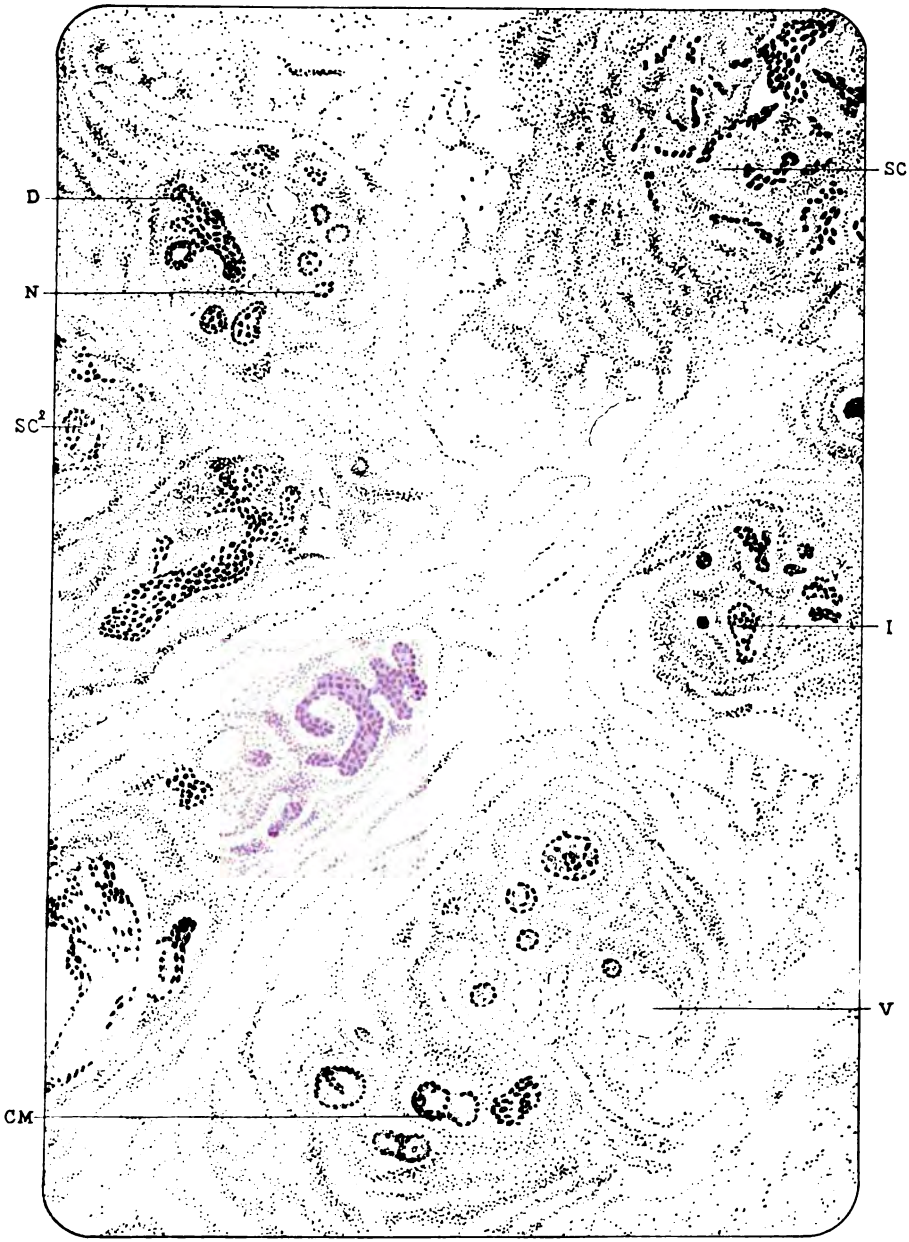
C M. Round cell-masses, with central part occupied by large and degenerated cells, the whole arranged in a distinct group.

N. Cell masses, little larger than normal gland acini, arranged like a breast nodule.

D. Large cell columns communicating with round masses.

V. Spaces where cell masses have fallen out.

I. Cell masses intermediate between those of C M and S C.



Cecil F. Headlee, del.

Dawson & Cochrane, Ltd.

DESCRIPTION OF PLATE VII.

Illustrating Mr. Cecil F. Beadles's communication on some Histological Changes in the Breast found in association with Glandular Carcinoma. (Page 175.)

From drawings by the author.

FIG. 1.—Breast tissue from a case that contained two distinct carcinomatous growths, each the size of a small walnut, and proving microscopically to be scirrhus. (Zeiss obj. AA.)

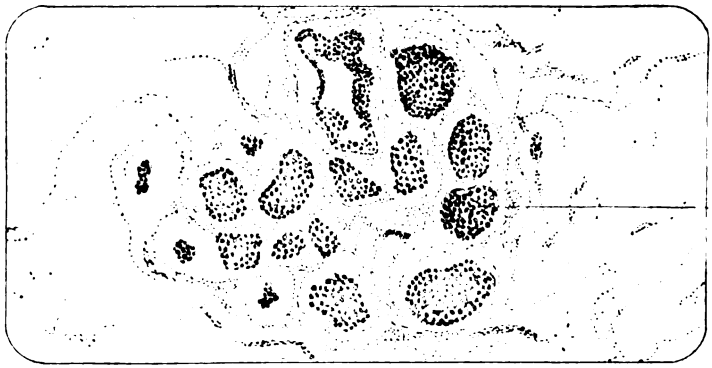
The breast symptoms were of nine months' duration.

There is very little change seen in the stroma around the breast lobules or elsewhere.

L. Large cell masses arranged in lobules. The nuclei of the epithelial cells are mostly round and of a uniform size.

FIG. 2.—The cell mass shown in Plate VI, C M, highly magnified. Small cells surrounding degenerate mass, in which some cells of large size are seen. (Zeiss obj. E.)

FIG. 3.—The cell masses N in Plate VI highly magnified. (Zeiss obj. E.) These alveoli are very little larger than normal acini. They are filled with epithelial cells varying in size and irregularly arranged. The smaller cells are the size of glandular epithelium; some are degenerated.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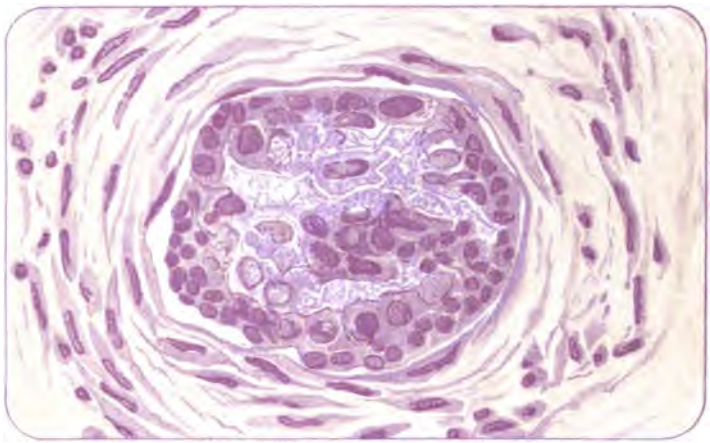
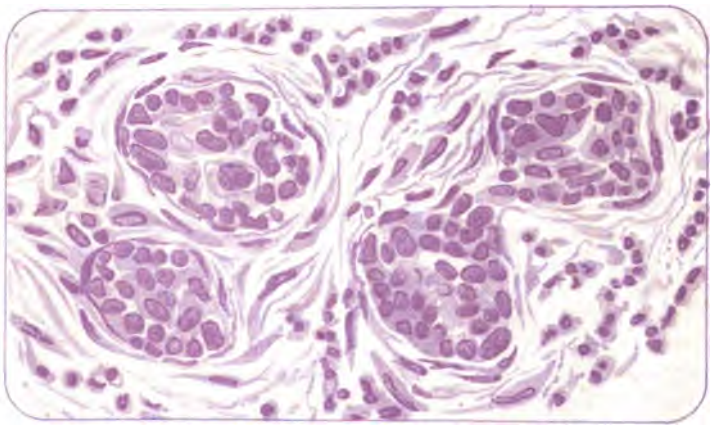




DESCRIPTION OF PLATE VIII,

Illustrating Mr. Cecil F. Beadles's communication on some Histological Changes in the Breast found in association with Glandular Carcinoma. (Page 175.)

From drawings by the author.

FIG. 1.*—From a breast containing a small, hard, scirrhous growth of nine months' duration, the size of a thumb nail, and of infiltrating character. (Zeiss obj. A).

Spaces irregular in shape and lined by larger columnar cells, and separated from one another by narrow bands of fibrous tissue.

I. Small papillomatous ingrowths.

P. Spaces containing intracystic growths of considerable size.

D. Degenerated epithelial cells.

FIG. 2. From a breast that contained two distinct carcinomatous tumours. The first was of six months' duration. Microscopically the growths contain small epithelial cell masses. One tumour was the size of an egg, the other that of a walnut. (Zeiss obj. 4·0 mm. Apochromat.)

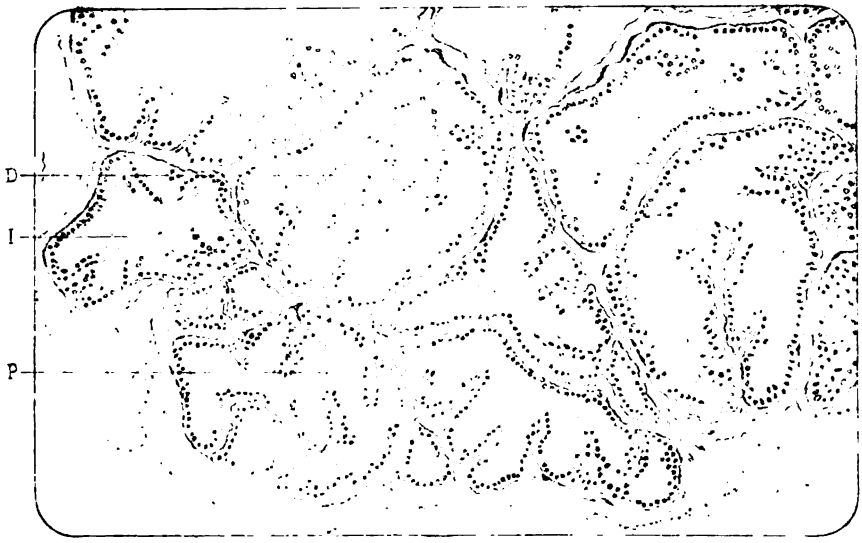
Spaces from a group of such, lined by columnar cells and containing intracystic growths.

I I. Intracystic growths of connective tissue.

D. Intracystic growth, the stroma of which is composed of swollen and degenerate cells.

E. Part of epithelial lining of a cystic space.

* In the description of these figures in the text Fig. 1 is referred to as Fig. 2 and Fig. 2 as Fig. 1.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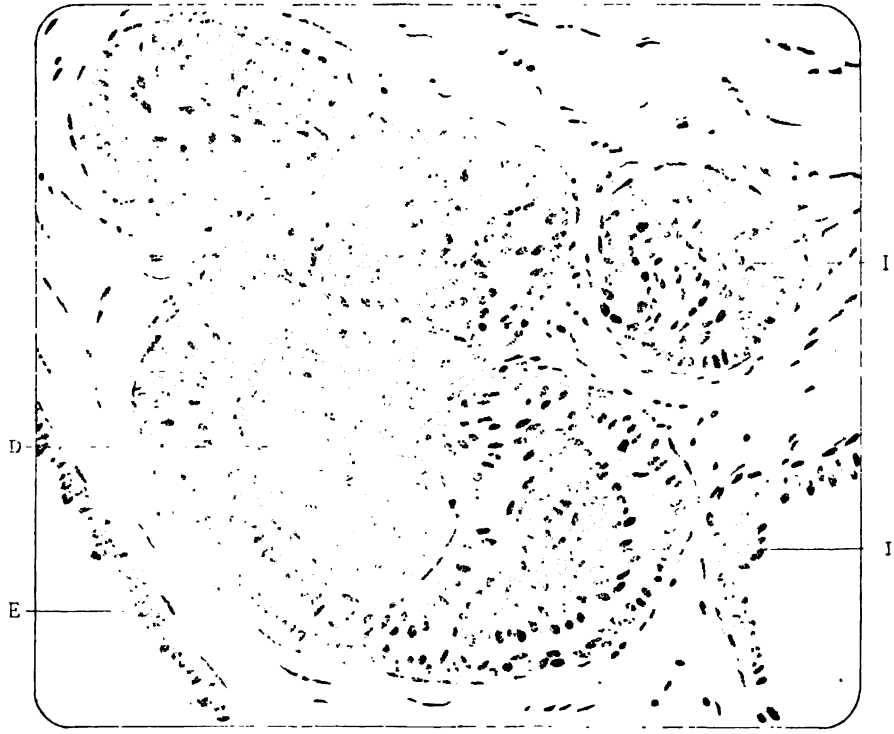
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columns have all the appearance of the collecting ducts into which the acini open, the lumen of each having become filled with cells. That these cell-masses are not prolongations in the lymph channels from the larger growth is clear both from their peculiar grouping, and from the fact that in many cases no communication between the two could be found in the intervening tissue. It is important to note that the alteration in the epithelium may be very extensive without corresponding changes in the stroma.

Here, then, we have in these thickenings and in the neighbourhood of the small nodules, as well as elsewhere, a condition of the breast which is obviously intermediate between simple adenoma and glandular carcinoma, extremely suggestive of commencing malignant disease. To make the picture more complete we may find an alveolus in which the walls have given way, and the cells form an irregular mass projecting into the stroma between the connective-tissue fibres. Gradual transitions can be found between such outgrowths and the actual formation of a minute scirrhous nodule. This process is especially seen where the primary tumour is of the kind known as true scirrhus. Often where the growth is of a more encephaloid nature we are able to trace the gradual enlargement of groups of acini containing irregular and enlarged cells. These form distinct lobules, and although the acini have attained a very large size they still retain a perfectly normal position relatively to each other. Notwithstanding this arrangement, no one would hesitate in pronouncing one of these larger groups as being a small nodule of carcinoma, in which the epithelial element greatly predominated. With these facts before one, it is not unreasonable to imagine that the nodules of carcinoma found at a distance from the tumour are not necessarily secondary growths merely, but may be primary, due to the same cause as that which gave rise to the larger tumour. Whether the smaller nodules have all arisen later than the large growth, or at the same time as the larger mass, but growing more slowly, it is impossible to say.

Papilliform changes in the epithelium of ducts.—There is another condition of which I have yet to speak, namely, a peculiar change affecting the ducts. We may not infrequently find in sections from the breast tissue a group of spaces surrounded by denser tissue, which, when large, may be felt as distinct nodules (Plate VIII, fig. 2). The spaces vary much in size; those that are small are round or oval in outline, but as they become larger they lose

their regular form, and become separated from one another by a few bands of fibrous tissue only, and small processes pass into them from the fibrous stroma. But it is the epithelium lining these spaces that is the seat of a characteristic change now to be detailed. The epithelium is composed of a single layer of columnar-shaped cells of very great size, arranged evenly upon the basement membrane, and covering the small papillomatous ingrowths of the stroma. The cells have a granular appearance, and stain in a peculiar manner with logwood. The peripheral end is somewhat expanded, and situated towards the attached end of the cell is a round nucleus somewhat larger than that of a normal cell of a duct. In the neighbourhood of these spaces ducts may usually be seen which are lined by healthy columnar cells of normal size. Groups of spaces much the same as those just mentioned, but not possessing the ingrowths, may be found, in which the lumen is filled with degenerated cells, and contains some of the yellow-coloured globules before referred to.

There appears to be nothing of a malignant nature in these large columnar-shaped cells arranged in this papilliform manner, and this same condition may be found in the breasts of women of an equal age, which contain no form of malignant growth. Creighton ('Report of Medical Officer of the Privy Council and Local Government Board,' 1875, p. 178) has also described and figured this papilliform change in the ducts of the breast in a bitch co-existent with a mammary tumour.

Besides the above-described condition there is another sometimes met with, which I have seen only in breasts the seat of carcinoma, but which naturally may not be necessarily dependent upon the co-existence of the latter. In this second variety of papilliform change we see a group of spaces lined by columnar cells, which are enlarged only to a moderate degree, and stain naturally with logwood (Plate VIII, fig. 1). The smaller of these have only a single layer of healthy epithelium lining them, but in those that are larger there is seen in some a fine branching process of fibro-cellular tissue spreading in from beneath the columnar cells. This may be developed to such an extent as to completely fill the lumen, and we have an intra-cystic growth, in which the stroma is represented to a very slight degree, being in some cases hardly perceptible. In adjoining spaces all stages of degeneration may be seen; in some the cells of the stroma are greatly swollen out, in

others they have lost their distinctive outline and nucleus, and at last there is only a homogeneous structure left, in which all trace of the stroma cells has gone, and which has the same look and possesses the same manner of staining as does the stroma of fibromata of the breast, or the stroma of many scirrhous growths. The epithelial cells under these circumstances have long since disappeared.

Conclusions.—In the foregoing remarks I have endeavoured to show that the portion of the breast which is external to a primary carcinomatous tumour, is by no means in a normal condition. That, as has been suggested by others, the acini show proliferative and other changes in the epithelium. I find that in addition there are profound alterations of the stroma, and further believe that my specimens show ground for regarding these disordered conditions of the gland to be independent of the primary growth, so far as direct infection is concerned. Here I may add that the occurrence of such direct infection, except in the immediate neighbourhood of the tumour, is, in my experience, very rare, and I have excluded it in the instances of the changes described above as peripheral.

The existence of such wide-spread alteration of the rest of the gland not having been generally appreciated, it would seem that we must revise our ideas of the nature of the invasion of the breast by cancer, and we must keep our minds open as to how far the primary growth is the direct causative factor in evoking these peripheral changes, or how far the latter are due to the original cause which produced the primary growth.

Finally, the facts I have described tend to show one cause of what are called recurrences, where the breast has not been removed or not entirely so, and add their weight to that of many others for the entire and very careful removal of all traces of breast tissue, when there is carcinoma present in the gland.

January 5th, 1892.

X. MISCELLANEOUS COMMUNICATIONS.

1. *A case of myxœdema associated with tubercular disease of the lungs and larynx.*

By Hector W. G. Mackenzie, M.D.

A woman aged 38, who for five years had suffered from symptoms of myxœdema, was admitted to the Royal Free Hospital under the care of Dr. West.

At one time, it was said, there had been great swelling of the abdomen, arms, face, &c. She had the slowness of thought, perception, and action, and clumsiness of movement, of typical myxœdema. She had also the typical physiognomy—thick, immobile features, scanty hair, and flushed cheeks. While in the hospital she suffered from hallucinations at night. After she had been in the ward a fortnight she died one day rather suddenly after a meal.

At the *post-mortem* examination no œdema was anywhere present. There was no excess of subcutaneous fat. The flush on the cheeks had quite disappeared, the face being pallid. The lungs were very extensively affected with tubercular disease. The greater part of the right lung was consolidated. In the upper lobe there were cretaceous masses embedded in fibrous tissue, and near the apex there was a superficial pus-containing cavity about the size of a walnut. The lower lobe was solid from a combination of recent broncho-pneumonia and caseous tubercle. The pleura was much thickened, and was here and there dotted with tubercle. The left lung was similarly affected, but not nearly so much so as the right.

The larynx generally was much swollen from œdema. The epiglottis was turban-shaped, and was ulcerated on its under surface. There was pyriform swelling of the ary-epiglottic folds. The uvula and the pillars of the fauces were swollen. The mucous membrane of the commencement of the œsophagus was studded

with miliary tubercles, and in this situation there was also a small superficial ulcer. In the upper part of the trachea there was some caseous material, probably food. The thyroid gland was very small, pale, and soft. The liver was large, weighing nearly 60 oz., but did not appear abnormal. The spleen was large and soft. The kidneys were normal. The heart muscle was pale, and the wall was thin. The abdominal muscles were extremely pale in colour. The brain was normal. There was slight deposit of urate of soda in the great toe-joints.

The interest of the case is twofold. In the first place, there was no sign of either fluid or solid œdema except in the larynx and pharynx, where the tubercular disease was sufficient to account for it. The subcutaneous tissue as well as the skin seemed, in fact, drier than normal. The history pointed to there having been œdema at an earlier stage of the disease. In the second place, there was the association with tubercle which has been found in other cases of myxœdema. In the cases reported on by the committee of the Clinical Society there was a family history of phthisis in 27 per cent., and tubercle was found in at least three out of the fifteen cases on which the pathological portion of the report was founded. Myxœdema can, therefore, certainly not be included among the diseases, if any such exist, which are naturally prophylactic against tubercle. The number of recorded cases is, however, too few to come to any conclusion as to whether the disease predisposes to tubercle. It would be interesting to know whether cretins are more susceptible to tubercle than others. It has been stated that tubercle is almost unknown among patients affected with goitre.

October 20th, 1891.

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2. *A case of leprosy.*

By Herbert Larder and G. Thin, M.D.

H. S—, aged 19, who died on November 30th, 1891, was born in Barbadoes of English parents with no suspicion of leprous taint. As a child he used to frequently play with a leprous beggar, and when he was six years old some smooth livid spots

were noticed on his body. When eight years old he was sent to England, and during the last eleven years he was constantly under observation in University College Hospital and in the London Hospital, and was a patient at the Whitechapel Infirmary from July, 1885, until his death.

On admission he was in a weak condition, and covered with numerous sores, but recovered to a great extent, only a few sores being left on the face, hands, and feet. The good effect appeared certainly to be due to the employment of chaulmoogra oil, which was administered internally and used as a dressing to the sores. After the first few weeks the patient was able to get up, and even to go out in warm weather, until six months before his death, when an apical pulmonary affection declared itself with a constant cough, and he died from diarrhœa with exhaustion. The face showed very clearly the ordinary appearances of tubercular leprosy, and the limbs also. There was, however, but little deposit or ulceration on the surface of the trunk. There was a small patch of anæsthesia on the chest, and towards the end of life there was very great contraction and scarring of the lips and mouth, and he had frequent attacks of dyspnœa, apparently due to laryngitis.

At the *post-mortem* examination there was marked recession of the tubercles of the face. The glottis was greatly decreased in size by contraction and puckering of the epiglottis and vocal cords. There had been ulceration of the edges of the epiglottis and adjacent parts of the vocal cords, which had caused adhesions, leaving only a small rounded opening. The bronchial glands were enlarged, hard, and matted together. The lungs were infiltrated with nodular deposit, indistinguishable by the naked eye from tubercle, and the upper lobes were firmly adherent to the chest wall. The upper and middle lobes of the right lung had broken down into several small cavities, and so had both lobes of the left lung. The spleen and liver were enlarged, the genital organs small and undeveloped. The ulna and median nerves on both sides were much thickened, and of a brown colour below the middle of each forearm; and the perinæal nerves were found to be in a similar condition, though to a less marked extent. The other abdominal aud thoracic organs were normal in appearance, as were also the brain and spinal cord.

The subjoined report upon the microscopical appearances of the tissues has been kindly furnished by Dr. G. Thin.

Report of microscopical examination by Dr. Thin.—The only

PLATE IX.

Illustrating Mr. Larder's and Dr. Thin's case of Leprosy in a youth aged 19. (Page 185.)

Danielsson & Co., Photo Print.

point of special interest in connection with the case of this boy is the condition of the lungs. The distribution of leprosy bacilli in the skin and other organs presented nothing unusual, and the demonstration of the bacilli in the testicle only confirms what has been already observed in previous cases. As regards the lungs, the question is whether in the disease present there is a leprous infiltration of the lung or the infiltration of ordinary tuberculosis, and whether the bacilli found in the lung tissue are leprosy bacilli or tubercle bacilli.

The naked-eye appearances, to the best of my judgment, did not differ from those characteristic of ordinary tuberculosis; and after careful study of sections kindly prepared by Mr. E. Henderson and Mr. Andrew Pringle, I have come to the conclusion that the bacilli in the lungs are not leprosy bacilli, but tubercle bacilli. Mr. Pringle has arrived at the same conclusion.

It is a matter of considerable pathological interest that in a patient whose tissues harboured such numerous masses of leprosy bacilli, the lungs should contain none, but should be found the seat of tuberculosis produced by the bacilli of tubercle. I therefore sent two of Mr. Pringle's sections of the lung to Dr. Hansen, of Bergen, who has been so good as to favour me with the following opinion:

Dr. Hansen remarks that after close examination of the two preparations he considers himself authorised to say that they are not from a leprous lung, but from a tubercular, and on the following grounds. "I quite agree with you," he remarks, "that it is impossible to tell whether you have a leper bacillus or a tubercle bacillus before your eye; but I will say that I never have seen a leper bacillus curved, although I have often seen tubercle bacilli of this form. In your preparations there are many curved bacilli; and some very long, much longer than leper bacilli ever become. On these grounds alone I would not venture to declare the bacilli to be tubercle bacilli; it is specially the arrangement of the bacilli that induces me to say that they are not leper bacilli. It is only in the edges of the preparations that the bacilli occur, and here they are spread out just as tubercle bacilli in sputum. It gives me the impression that you have got the wall of the cavity in the sections, and in these places the bacilli are, as you know, very abundant. In the lung tissue itself I can see none. Further, you will know that the leper bacilli always lie together in

clumps in the leprous growths or in the cells. You can sometimes find the bacilli spread over small areas, but you will always at the same time find them clustered together in small clumps."

Dr. Hansen goes on to remark that the description of the condition of the bronchial glands would have aided him in forming an opinion, the appearances of leprous and tubercular glands being so different that it is impossible to be in doubt what you have before you. He adds that in former years there was much tuberculosis amongst lepers in the asylums, but that in latter years it is very rare, although tuberculosis is spreading greatly throughout Norway. He attributes the diminution of tuberculosis in the leper asylums to the smaller number of patients they contain, the greater purity of the air, and the diminution of the facilities for infection by tuberculosis. He mentions that he once inoculated two apes with leprous tissue, and kept them in the *post-mortem* room, where they died of tuberculosis, attributable, he believes, to infection acquired in the room in which tubercular lungs of lepers were frequently examined. He adds that he has seen much intestinal tuberculosis in lepers, but always found the mesenteric glands tubercular, and never leprous.

In the tissue from the lung in this boy's case I found, as Dr. Hansen states, that the bacilli were chiefly present in the fibrous tissue surrounding the lung tissue proper; but I also found in some sections a few bacilli a certain distance in the proper lung tissue.

I base my opinion that the bacilli in the lung are tubercle bacilli, and not leprosy bacilli, chiefly on the fact that the characteristic arrangement in clumps of leper bacilli is absent.

December 15*th*, 1891.

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3. *Cultures and preparations of bacilli from cases of leprosy. (Card specimen.)*

By Chas. Slater, M.B.

Cultures and preparations of bacilli isolated from cases of leprosy by various observers were shown. They included all the organisms which have any serious claim to be considered identical

with the bacillus found in leprosy tissues. None of the cultures have as yet given any positive results on inoculation. The specimens shown were—

1. A culture and preparation of a bacillus isolated by Prof. Bordone Uffreduzzi from the bone marrow of a patient who died of tubercular leprosy. The organism resembles closely in size, shape, and staining reaction the bacillus found in the tissues.

2. A culture and preparation of a bacillus identical with the above, isolated by Prof. V. Gianturco from a non-ulcerated nodule.

3. A culture and preparation of an anaërobic organism, obtained on three occasions from two cases by Prof. R. Campana. This organism is decolourised by Ehrlich's method.

4. A preparation of an organism isolated by Drs. Beaven Rake and Buckmaster from the serum of a blister formed over a non-ulcerated leprous tubercle. This organism retains the colour when stained by Ehrlich's method. *March 1st*, 1892.

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4. *Inoculated tuberculosis in snakes.*

By Walter K. Sibley, M.D., B.C.Camb.

[With Plate I, fig. 2.]

Since publishing a description of a case of spontaneous tuberculosis in a snake in 'Virchow's Archiv,' in 1889, I have been working at the artificial production of tuberculosis in reptiles and other lower forms of animal life by inoculating them with tubercle bacilli.

While working in the laboratory of Professor von Recklinghausen in Strasburg I kept various cold-blooded animals, such as snakes, blindworms, lizards, salamanders, newts, and frogs, inoculated with tubercle at high temperatures. The only results derived from these experiments were some with regard to the temperatures at which these animals may, under certain circumstances, be kept alive. In no case was it possible to demonstrate the presence of tubercle after death. Upon my return to this country, and while waiting for the necessary permission from the Home Secretary to

perform experiments upon animals, I employed my time in inoculating some of the invertebrate forms of animal life, these not coming under the sympathy of the Act. Amongst others, I found that it was possible to keep certain kinds of land snails for a considerable time at temperatures quite high enough for the bacilli of tnbercle to grow. Here, again, my experiments gave but negative results as far as tuberculosis was concerned, but some very interesting ones with respect to the temperatures.

The more recent experiments were begun at the Brown Institution, with the kind permission of Mr. Victor Horsley, but owing to difficulties in methods I was again never able to produce the disease, the snakes always dying shortly after the inoculation, and before there was time for tuberculosis to show itself.

The experiments I am about to describe were performed at the Bacteriological Laboratory at King's College, with the kind permission of Professor Cruickshank, to whom I am much indebted for many valuable hints. The snakes used were the common English ring snake and the common viper.

In a former paper it was noted that the temperature of the reptile-house at the Zoological Society's Gardens was somewhat below that at which the bacilli of tuberculosis were then considered to be able to grow, as originally stated by Koch, viz. 30° to 40° C. More recently it has been shown that the bacilli can be grown at a much lower temperature than this, even as low as 20° C., but that the growth under these conditions is very much slower; in fact, it may be many weeks before there is any sign of growth at all.

Having inoculated the snakes with pure cultures of tubercle bacilli grown on agar-agar and glycerine, they were placed in incubators regulated for a temperature of about 33° C. Under these circumstances it was found that the reptiles died within a few days, and it was some time before the cause of death could be ascertained. Was it due to the inoculation, or to the temperature, or to some other cause? Having previously kept snakes in good condition at much higher temperatures than these, the temperature was excluded; so also it was found that the snakes could be freely inoculated and kept in the ordinary way without any ill effects. The clue was obtained by observing that the snakes died in great numbers on Sundays, or rather were found dead on Monday mornings, that is, after the incubator had been closed longer than usual.

From this it became evident that the snakes died from a process of suffocation. After this they were kept in glasses open at the top, and so could get plenty of air. These glasses were placed in a large zinc bath half full of water. The temperature of the water in this bath was maintained at about 35° C. by means of a small regulating gas burner placed underneath. From this time the inoculated snakes did very well, and were fed regularly with frogs once a week, or more frequently as circumstances required.

After many negative attempts I finally succeeded in producing tuberculosis in four cases, two of which will be described under the letters B and C.

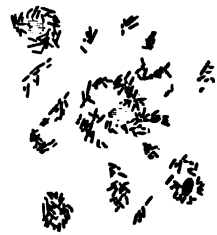
Snake B.—Inoculated with pure culture of tubercle bacilli on June 14th, July 8th, and July 22nd, 1890. The reptile died on August 5th, that is to say, fifty-two days after the primary inoculation. There was but little change to be seen in any of the internal organs with the naked eye. The liver contained some exceedingly minute specks, and the lung in its middle third had considerable degeneration and necrosis of its lining endothelium, together with some miliary deposits scattered about on the internal surface of the same. The tissues were hardened in alcohol and cut. Microscopically the liver, examined without previously staining, showed a number of small, dark, exceedingly granular areas, each consisting of some ten to thirty round cells, containing in their interior a very granular and pigmented material, the pigment being of a dark brown colour. These groups were most of them round or oval, and scattered irregularly throughout the organ. On the addition of an acid the outlines of the cells in them were rendered more distinct. With picro- or alum-carmine these cells stained much less readily than the other cells of the organ. With Neelsen's method each of these granular cells was seen to contain numbers of tubercle bacilli.

But little change was to be discovered in the pancreas. No bacilli were to be demonstrated with Neelsen's stain, but some few rather large bacilli were brought out with Gram's method.

The lung showed small deposits with regular margins on the internal surface of the alveoli, composed essentially of granulation tissue with central caseation in some areas. A very few epithelioid cells were seen; these were in irregular groups, and apparently arose from the endothelium of the pulmonary alveoli. The process of inflammation was seen to extend first along the surface of

the septa between the several alveoli. In most parts these caseous deposits were crowded with tubercle bacilli, and in many places groups of large micrococci were also present, as shown by Neelsen's stain and double staining with methylen blue, the tubercle bacilli being then red and the micrococci blue. In some other parts of the lung tubercle bacilli were seen in great numbers in isolated groups. Each group apparently consisted of a cell (leucocyte) filled with bacilli, many of these cells having two or more nuclei, and in most cases the bacilli formed a complete ring round the nucleus. Thus in examining a large area there appeared a number of small rings of bacilli, each ring isolated and distinct from its neighbour (see Fig. 14); nor did there appear to be any scattered

FIG. 14.



Showing arrangement of the tubercle bacilli within the leucocytes, often in rings around the nuclei (the outlines of the leucocytes are not shown). Zeiss, $\frac{1}{12}$ oil immers., oc. 4.

bacilli in the tissues about—that is, none were seen outside the leucocytes. In other parts, where more extensive inflammatory changes had taken place, very large densely packed areas of bacilli were seen. All about these central groups, apparently formed by the coalescence of a number of isolated cells, there were seen many outlying cells filled with bacilli, and here there were also a few isolated bacilli apparently lying in the tissues outside the cells. These bacilli were usually very large. In all of these areas of change the alveoli of the lung were filled up with granulation tissue.

On examining a layer of the serous membrane surrounding the lung (pleura) the whole substance of this was densely infiltrated with small round cells, each one full of tubercle bacilli, and in places these cells were becoming fused into larger masses.

Snake C.—Inoculated with a pure culture of tubercle bacilli on June 14th, July 8th, and 22nd. The reptile died seventy-one days after the first inoculation. With the naked eye very little change could be detected.

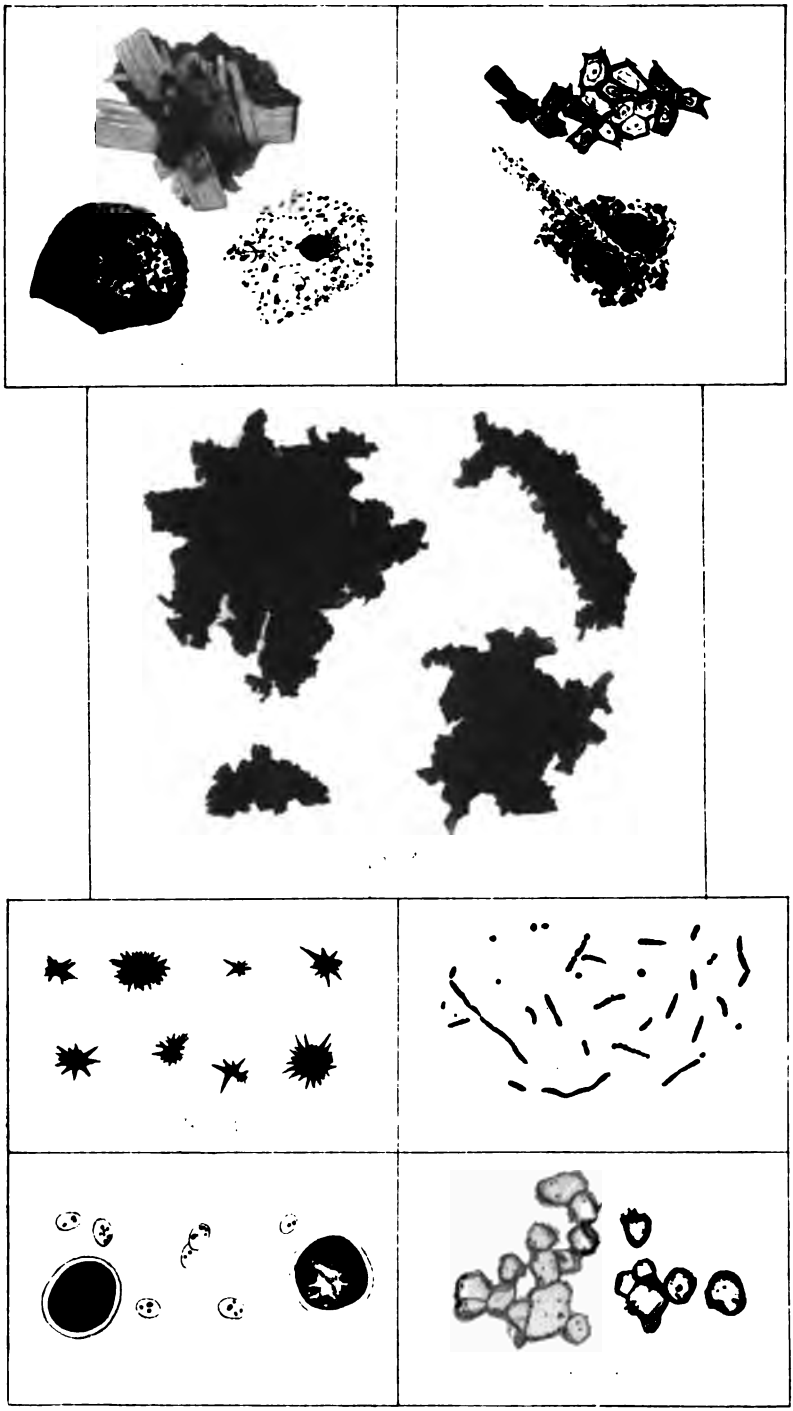
Microscopically, no deposits were found in the lungs or pancreas. The liver when examined unstained presented a number of small roundish pigmented deposits, larger than those seen in the Snake B just described. These areas consisted of a number of small round cells, nucleated and exceedingly granular. In some parts of the liver the deposits were in the walls of the larger branches of the portal veins. Some occurred within the lumen of the vessels, others were scattered throughout the gland. The general appearance of the deposits was much as described in the previous case, only the areas were larger, containing a greater number of small round cells filled with bacilli. The spleen also in this case contained a few deposits of the same nature, the cells of these being nucleated, very granular, pigmented, and filled with tubercle bacilli.

With regard to the bacilli in these cases, they stain readily with the aniline dyes, such as fuchsine and methylene blue, so also with the carbolic acid fuchsine of Ziehl or Neelsen, in all cases resisting the action of acids (30 per cent. nitric acid or 5 per cent. sulphuric acid), and maintaining the dye after treatment with the same.

A question that might be raised in connection with these experiments is, has the disease recognised as tuberculosis been produced, or have we only obtained cultures of tubercle bacilli grown in the animal's body? In other words, would it not be possible to conceive of the snakes as test-tubes, containing a nutrient medium in or on which the tubercle bacilli have simply grown? From the description it was seen that deposits containing bacilli occurred in many of the internal viscera, such as the liver, lung, and spleen. These deposits consisted for the most part of groups of tubercle bacilli within the substance of leucocytes, and these latter occurred in some places isolated, and in other parts in groups. In the liver, for instance, there were scattered throughout the whole organ groups of cells filled with bacilli. Before attempting to answer this question we must determine what constitutes a tubercular deposit or granuloma. Tracing the origin of such from these experiments, it would appear to be much as follows:—In the first place, a specific irritant, a tubercle bacillus, is present in the tissues;

this bacillus, we may suppose, either finds its way into, or is eaten up by, a leucocyte, according to whichever theory we accept regarding the relation of the cells to the germs. The bacillus within the cell then reproduces itself, or the cell takes up more bacilli, and thus, in one way or the other, the cells become more or less filled with bacilli. Next the several cells, each full of bacilli, collect together in groups. At first the presence of the leucocytes filled with bacilli produces little or no influence upon the surrounding structures; in time, however—in fact, as soon as the leucocytes begin to degenerate and die—a certain amount of inflammation occurs around, soon shown by the presence of a zone of small round cells. In the course of time other changes are set up in the tissues, both those with the bacilli-containing cells and also those immediately around these, forming at last granulomatous masses of various sizes.

Where then, it might be asked, in the above process does tuberculosis as a specific disease begin and cultures of the bacilli cease? To illustrate the point in question, if, instead of actively growing organisms, an inorganic substance—as for instance, carmine—be injected into the body, this would be taken up by the leucocytes, and there would be found carmine-filled leucocytes. If now this carmine substance within the cells could reproduce itself, should we, as the result of the increased irritation, get a granuloma—in fact, a "carmine granuloma." The tubercular granuloma of older writers consisted essentially of three zones, a central giant-cell surrounded by epithelioid cells, and these by small round cells or granulation tissue. As the result of the study of comparative tuberculosis modern pathologists have given up the idea that all three of these zones are essential to the tubercular deposit. At first it was found that the giant-cell was not always present, and then that even the detection of epithelioid cells was not of much significance. In some of the cases above described all that is seen is a cell filled with tubercle bacilli, then many similar cells grouped together and each one full of bacilli, and then the same group of cells surrounded and impregnated by some small round cells. In the case of the lung in the second snake described there was seen, in addition to the groups of leucocytes full of bacilli undergoing degenerative changes, some inflammatory area around—in fact, here constituting a true granuloma. It therefore appears impossible to say, in tracing through the various stages in these speci-



DESCRIPTION OF PLATE X.

Illustrating Dr. Ord's paper on Deposits of Indigo from Urine. (Page 195.)

FIG. 1.—The blue masses from Mr. Clutton's specimen, deposited, without use of reagents, from alkaline and offensive urine (× 210.)

FIG. 2.—Cells of stratified epithelium, stained by nascent indigo, the nuclei more deeply so than the rest, together with clusters of uric acid crystals, encrusted with and partly stained by indigo.

FIG. 3.—Portion of surface film of indigo artificially deposited in urine. Flat crystals, apparently of uric acid, slightly stained and strongly outlined by the pigment. Also structures resembling epithelial scales, with nuclei, stained, and occupied by granules of indigo. (× 510.)

FIG. 4.—Hedgehog crystals of uric acid deeply stained by indigo. (× 510.)

FIG. 5.—Bacterium (?) deeply stained by nascent indigo. From urine of case of tubercular peritonitis. (× 510.)

FIG. 6.—Yeast and starch-granules from indigo-yielding urine, containing also iodide of potassium. The yeast has the indigo stain, the starch has the iodine stain. The yeast, &c., were added to the urine before chemical treatment. (× 510.)

FIG. 7.—Flat discoid crystals from surface film of artificially deposited indigo, from urine of tubercular peritonitis. (× 510.)

mens, where a granuloma is present and where it is not—in fact, where natural cultures of tubercle bacilli within the body end and tuberculosis as a specific disease begins.

After the case of spontaneous tuberculosis in a snake described in a former paper, and the results of these experiments, tuberculosis can no longer be considered a disease confined to the higher, or warm-blooded animals. The same disease, under certain circumstances, can be produced in cold-blooded ones. In fact, I see no reason why it should not also be artificially produced in some of the Invertebrata; and, as mentioned in the beginning of this communication, I have already carried on some experiments in this direction, the details of which I hope to publish before long.

November 17th, 1891.

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5. *Deposit of indigo in the urine, with experiments.*

By William M. Ord, M.D.

[With Plate X]

I am indebted to the kindness of my colleague Mr. Clutton for the preparation which forms the basis of the few observations which I have to make, and to my colleague Mr. Shattock for much valuable help in the mounting of illustrative microscopic slides. It is a preparation showing indigo deposited in the urine before passage; that is to say, so far as is known, without the intervention of any chemical agency other than those which the body may contribute.

The specimen as seen under a quarter-inch objective presents numerous masses of a deep blue colour exactly corresponding with the colour of indigo. The masses are of irregular shape, some roughly quadrangular, others branched, the branches running straight from a common point, but with no regular radial arrangement. On the margin the surface, whatever its form, is studded with minute, sharp-pointed projections, in which the blue colour

is clearly seen. The substance is completely opaque and practically black. The impression conveyed by these objects is that they are composed of some crystalline material partly stained by indigo, partly having indigo in a non-crystalline form deposited on them. The bodies were found in the urine of a man aged 64, who had suffered for ten years from symptoms indicating enlargement of the prostate and imperfect emptying of the bladder. The patient appears to have consulted, at one time, Dr. Pavy, who remarked that he was a "manufacturer of indigo." On December 8th, 1891, the patient consulted Mr. Foley, of Forest Hill, on account of "dribbling" from the bladder. Mr. Foley found the bladder distended up to the level of the umbilicus. Hitherto no catheter had been used. A catheter being now passed, the urine was found to contain large flaky masses, some of which were brought to Mr. Clutton for examination. The masses are described as being like the lining of a sebaceous cyst. The urine was alkaline and very offensive. Under the microscope the masses were found to be really altered mucus, and to contain embedded in them a large number of the blue objects already described, together with triple phosphate and urates. After frequent washing out of the bladder the appearances altered. Mucus remained, but the dark blue bodies had disappeared.

In March, 1892, Mr. Clutton performed supra-pubic cystotomy, the prostatic obstruction having become excessive. So far as is known, no more indigo was passed. Mr. Clutton gave me the specimen because he knew that I was much interested in the meaning and result of the appearance of indigo in urine. Some years ago, when Dr. Murchison was president, I had the honour of exhibiting to this Society a calculus containing a large quantity of indigo found *post mortem* in the pelvis of a kidney. This was the first specimen of the kind found, or at least recorded. Since then Professor Chiari, of Prag, has published accounts of two indigo calculi. From the discovery of the calculus my attention has been much directed to the presence of indigo in urine, and the indications which it might afford. Nevertheless no case in which blue indigo was passed in the urine has come under my observation. Prout and others have published observations of blue urine, originally supposed to be due to the presence of Prussian blue, but proved by Prout in the case observed by him to be due to indigo blue. When Mr. Clutton gave me the specimen I concluded, after careful

observation, that the indigo had partly stained, and had partly been deposited on, a previously existing subcrystalline mass, consisting either of urate or of phosphate. The form suggested urate produced by the action of carbonate of ammonia upon a mass of crystals of uric acid. It will be seen that the deposit occurred in alkaline urine. I know of no method by which indican, present in alkaline urine, may be decomposed so as to form indigo blue without inducing an acid reaction. So far, therefore, I was unable to imitate, in experiment, the process leading to the formation of the blue bodies. But considering the specimens, it appeared to me that the form assumed by the indigo was determined by the form of the substances upon which it had been deposited. Looking at the matter in this light, I determined to institute observations with regard to the forms which might be assumed by indigo artificially precipitated from urine. The method which I have used has been the addition to a given bulk of urine, not less than ʒj, of an equal quantity of fuming hydrochloric acid, free, as far as possible, of chlorine, with the subsequent addition of a drop of a weak solution of hypochlorite of soda or lime. Heat is produced by the admixture of the hydrochloric acid to the urine, and appears to be a factor in the decomposition which follows. If the urine contains any large quantity of indigo it assumes colours of various kinds, ranging from deep blue through bottle-green to greenish brown; sometimes it yields a dull red colour, in which case indigo is rarely deposited. The former solutions, being shaken with chloroform, impart to it a pure indigo-blue colour. If chloroform be not used and the mixture be allowed to stand, particularly in bright sunlight, a film is speedily found to have formed on the surface. Viewed by reflected light, the film has a metallic coppery lustre, like that of burnished indigo; in transmitted light it is perfectly blue.

Four years ago it occurred to my son, then my house physician, to examine one of these films under the microscope at St. Thomas's Hospital. He found it to consist of small discs, rather larger than red blood-corpuscles, not completely round, but presenting numerous facets joined by rounded angles. The bodies were, in their main substance, of an exceedingly pale yellow colour, and were margined by minute spherical dots of a blue colour. Each of them also presented a blue discoloration in the centre. Examined from various aspects the bodies appeared to be crystal-

line, and were easily dissolved in distilled water, the blue dots persisting. The only crystalline substance, which I can conceive as remaining after the action of strong hydrochloric acid, is uric acid. I gave at the time a slide of these forms to Mr. Shattock, who still possesses it. When I had to consider Mr. Clutton's specimen I determined at first to see what might be the effect of precipitating indigo in the presence of a distinct excess of uric acid. For the purposes of experiment I made use of the urine of children suffering from tubercular disease of the intestines, such urine being almost invariably rich in indigo. Here, in addition to the superficial film, I found at the bottom of the test-glass crystals of uric acid partly stained, partly incrusted by indigo. An excess of uric acid not being always present, I introduced in several cases a strong solution of urates. When I speak of the uric acid being stained, it is right to say that the staining was not uniform, but corresponded mainly to the striæ commonly seen in uric acid crystals. It was rather an interpenetration than a true staining, and in this respect corresponded with the central coloration of the discs already described in the film. Some of the forms so obtained bore a strong resemblance to Mr. Clutton's specimen in spite of the very different reaction of the fluid. In examining these deposits I found some other forms of great interest. I found that the cells of stratified epithelium were strongly tinged with the blue of indigo, the nucleus for the most part of a deeper colour than the rest of the flake, at the same time that the flake, far less generally stained, was in addition studded with fine spherical granules of an intense blue colour.

In some of my observations I found also minute thread-like bodies, looking like bacteria, and very deeply stained. They were sometimes rods with faint transverse markings, sometimes rods composed of minute spherules. At present I am unable to say what their actual nature may be. I think that they are not any kind of mycelium, but that they are actual bacteria, possibly proper to urine. I should be grateful if any bacteriologist could give me an opinion as to the nature of these bodies, which, as mounted by Mr. Shattock, can be seen under the microscope, and, as drawn by Mr. Lapidge, can be seen on the card passed round (see Plate X). In one or two cases I have added yeast to the urine before making the decomposition. The yeast-cells can then be seen presenting a sharp, unstained, oval outline, containing one, two, or three

irregular masses, deeply coloured, in the interior. Any associated starch granules are also stained, but the colour is purplish and is evanescent. There is another crystalline form to which I ought to draw attention. Sometimes what I suppose must be uric acid is deposited in hedgehog crystals, with long processes. These are always very deeply stained, so as to be almost black, and are also incrusted towards the centre.

In some cases, where the quantity of uric acid appears to be small, the surface, instead of being composed of crystalline bodies, is extremely thin, and almost homogeneous, although with high powers numerous small yellowish spots can be detected. I am indebted to my house physician, Dr. Latter, for some excellent preparations of this kind. It is also interesting to note that the films of either kind are often in part sublimed, communicating a purplish-blue colour to paper placed over the mouth of the test-glass, still more strongly to paper introduced into the glass and reaching down to a point just above the level of the liquid. Indigo, as is well known, sublimes at a temperature of about 150° F., but here the temperature was of course much lower. This phenomenon, which I have quite recently observed, will require further investigation.[1]

The points which I have put before you may, I hope, have some interest. I am inclined to think that, as regards urine, and perhaps as regards pathological products artificially mixed with the urine, we may have here a staining process of some use. I am working at this matter still, but you will understand that it is not every day that one comes across a urine rich in indigo, and I am bound to say also that the experiments can be only performed when the hydrochloric acid is of the proper purity.

In reviewing my remarks I may state, as indeed I stated when I read the paper, that it is apparently only in its nascent state that indigo has the power of staining protoplasmic matter. There is no staining if the cells of one kind or another are introduced even a short time after the mixture of the hydrochloric acid with the urine. I have since stained pus-corpuscles, which react very much like the yeast-corpuscles; also anthrax bacilli contained in a culture, but not when present in fine sections of infected tissues.

[1] It is probable that this reaction is due to iodine, set free from iodide of potassium, passed in the urine by persons taking the drug medicinally. For this suggestion I am indebted to Mr. Shattock.

Nor have I succeeded as yet with tubercle bacilli. The reaction, if successful, would of course be valuable in the diagnosis of tubercle of the kidney. *May 17th*, 1892.

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6. *Experiments determining the cause of phosphatic deposition in boiling urine, and whether Proteus vulgaris and Pyogenic cocci will induce the ammoniacal fermentation of normal urine.*

By Samuel G. Shattock.

The fermentation of human urine may be taken as synonymous with the hydrolysis of its urea, *i. e.* the conversion of its urea by the assumption of water, and subsequent decomposition into ammonium carbonate. For although the possibility of other fermentations is conceivable, the amount of its other solids individually is so small that any such others may be ignored.

So far as is yet shown, this simple change in urine, the conversion of urea into ammonium carbonate, depends under ordinary circumstances, upon the action of living micro-organisms; it is a proper fermentation.

Leube has shown that the products of pure cultures of *micrococcus ureæ* filtered through plaster cells are incapable of exciting ammoniacal fermentation. But a ferment was isolated by Musculus from the "highly alkaline urine occurring in cases of catarrh of the bladder" (Pflüger's 'Archiv,' Bd. xii, S. 216, 217).

Sheridan Lea ('Journal of Physiology,' vol. vi, 1885), in citing this observation, has been led into the error of taking it for granted that the ferment was obtained not from any micro-organisms, but from the chemical substances present in the urine used.

Musculus states that the precipitate obtained from such mucous urine does not contain any ferment cells such as are present in urine which has passed into alkaline fermentation by exposure to air, which Lea immediately afterwards construes into the statement that his (Musculus's) work rather proved, therefore (in con-

trast with his own), the isolability of an unorganised ferment from mucous urine which contains no ferment cells, than from the substance of the cells themselves.

The evidence of this is at present quite inadmissible, for the question as to whether such "alkaline urine containing mucus from cases of catarrh of the bladder" did or did not contain micro-organisms cannot be answered; and the evidence could hardly be else than defective since the only micro-organism mentioned throughout the discussion is a torula. The observation needs, in short, repeating with the light which a further study of bacteriology has thrown on the subject.

Sheridan Lea, working with urine in which ammoniacal fermentation had been set up by exposure to the air, found that the ferment is not shed into the fluid, but is retained in the micro-organisms, from which it can be separated after they have been killed by treatment with alcohol. In this his result is in accord with Leube's.

Pasteur was the first to show that healthy urine will not become ammoniacal if it be withdrawn in such a way that no contamination occurs; but, as is well known, Sir Joseph Lister confirmed and extended Pasteur's observation. Nevertheless this knowledge is by no means yet general amongst physicians and surgeons, and this is my reason for shortly restating it. To be sure, urea is an unstable body, but there is no evidence to show that anything which healthy urine itself contains can bring about its own fermentation.

When urine is extravasated in quantity in the tissue around the kidney, as after rupture of the renal pelvis or ureter, the extravasated fluid, as told by direct observation, does not necessarily at least undergo fermentation.

In a case of ruptured ureter described by Mr. Arthur E. Barker in a boy, the swelling, which had all the characters of a hydronephrosis, was, aspirated, and forty-five ounces of fluid withdrawn having all the characters of urine, though it contained a diminished percentage of urea, and albumen due probably to the flow of lymph from the connective tissue into which it had been extravasated, and later to that poured into the cavity from the inflamed tissue bounding the collection. The aspiration was repeated on six occasions at intervals of about a week with practically the same result. The diagnosis of ruptured ureter was con-

firmed by the excision of the kidney; the urine had been poured out into the areolar tissue behind the peritoneum, and there lay in a large sac formed by plastic inflammation.

Nor, again, does the fluid as it accumulates in simple hydronephrosis undergo any other changes than such as correspond with those just described. It may finally contain albumen and little or no urinary constituents, but whilst the distension is proceeding this may not be so.

Mr. Alban Doran records an excellent illustration in the last volume of the Society's 'Transactions.'

The distended kidney held three pints of a clear, pale yellow fluid of a urinous odour (sp. gr. 1008), and without albumen.

In the extravasation which arises from stricture of the urethra the urine is often foul before the extravasation occurs; the case is altogether different; or its extravasation is preceded by the formation of a perinæal abscess about the site of stricture, and this, as will be noticed later on, alters the aspect of the question. Nevertheless, as will appear from the experiments recorded in the present paper, it would be unwarrantable to assert that normal urine, when extravasated into the tissues, does not, under any circumstances, undergo ammoniacal fermentation.

Sir Joseph Lister's experiment ('Trans. Royal Soc. of Edinburgh,' 1875, vol. xxvii) consisted, as it is described in the 'Path. Soc. Trans.' (vol. xxix, p. 426), in superheating liqueur glasses covered with loosely fitting glass caps and beneath shades, in order to render them sterile. The shade and cap, when cool, are gently removed, and the liqueur glass is charged from a flask into which urine had been received, the flask having been previously superheated with its mouth plugged with cotton wool; before the urine is received into the sterilised flask the surface of the glans penis is washed with a 1 in 40 solution of carbolic acid. Under such circumstances the urine in the liqueur glasses, though protected only by the cap and shade, remains absolutely unchanged for an indefinite period.

I have many times repeated this simple but pregnant experiment with slight modification. The use of an intermediate flask is unnecessary. The urine may be received directly into the sterilised glasses, rejecting the first portion in order to flush out the urethra and remove whatever traces of carbolic acid may have clung about the meatus. That the use of the carbolic acid occasions no fallacy it

is easy to show; for if precisely the same method is adopted, but the glass be freely exposed for a time by the removal of the shade and cap, and then re-covered, fermentation will ensue in the course of a few days, and this even if a drop of the carbolic acid solution, 1 to 40, be purposely added—more than could possibly reach it in the experiment even were the first portion of the urine not rejected; and the experiment will at times succeed without the use of antiseptics at all.

The urine, whether acid or not, keeps perfectly clear; its mucus subsides, and it either remains quite unchanged or deposits crystals of uric acid which adhere to the sides of the vessel.

This deposition of uric acid which sometimes occurs, is often spoken of as arising from an acid fermentation. But though the urine in which such occurs be kept for an indefinite period, I have not found it to undergo any further change. And although it has been suggested that the increased acidity may be due to the action of an organised ferment, there is as yet no evidence adducible for it.

It was formerly supposed that the fermentation of urine was effected only by one particular kind of organism, the micrococcus ureæ. A like doctrine was held of other fermentations; each, it was assumed, was induced by one and only one micro-organism as specific or peculiar to itself.

At present this holds true of none. Even the alcoholic fermentation of sugar may be brought about by the toruloid growths of certain moulds, *Mucor racemosus*, &c., although the great agents are the yeasts. The same holds true of acetic and lactic fermentation, of the fermentation of proteid, or common putrefaction, and the like. And in the case of ammoniacal fermentation, although there is one organism which is particularly active, others will induce the same change.

From ammoniacal urine there have been isolated three chief micro-organisms capable of inducing active fermentation: *Bacterium ureæ*, the most active; the next in activity, *Micrococcus ureæ;* and a second micrococcus, distinguishable from the latter by its liquefying nutrient jelly, *Micrococcus ureæ liquefaciens* (Flugge).

The last mentioned was isolated independently by Dr. W. R. Smith ('Quarterly Journal of Microscopical Science,' 1887, p. 371). Others, having feebler properties, are noticed.

Leube and Graser (1885, 'Virchow's Archiv,' c, p. 540), in addition to *Bacterium ureæ* and *Micrococcus ureæ*, have isolated two bacilli and a sarcina.

Heraeus ('Zeit. für Hygiene,' 1886, pp. 215—221) isolated four bacilli capable of causing ammoniacal fermentation; three of these liquefied nutrient gelatine, and were therefore distinct from the organisms described by Leube and Graser.

The inquiry into the causes of ammoniacal fermentation may be undertaken in two ways: (1) by isolating, from urine in which ordinary fermentation has occurred after exposure, the organisms which have set up the fermentation; (2) by inoculating urine with organisms other than those isolable, and observing whether fermentation is set up. It is the second method that I have adopted in the experiments recorded in the present paper.

Fermentations generally are, under common circumstances, due to the action of particular micro-organisms. Nevertheless it is equally true that the chemical processes occurring in some fermentations and ferment actions may be brought about quite independently of micro-organisms, or unorganised ferments.

To recall a familar instance. Starch is converted by the action of malt diastase or of ptyalin into dextrine, and finally maltose. But by the action of dilute sulphuric acid, starch is converted into dextrine, and though the end product is dextrose, or grape-sugar, maltose can also be formed as an intermediate product.

But apart from this, purely physical agencies will effect results like those brought about by fermentation or ferment-action.

By heating starch solution at 160° C. it is changed into dextrine, and after prolonged heating into dextrose or grape-sugar. Again, the process of gastric digestion is imitable by a similar method. Albumen by continuous boiling, or more readily by the action of superheated steam, is converted into albumose. The natural process of fermentation and that induced artificially are both examples of a similar chemical change, hydrolytic decomposition.

I come now to the question, is the hydrolysis of urea producible by any like method, *i. e.* one in which neither micro-organisms nor their products play any part? It is a curious fact that so common an observation as the deposition of phosphates, which comes about in urine under certain circumstances by boiling, has never yet received a satisfactory explanation.

If urine which is alkaline, neutral, or faintly acid be boiled in a

test-tube or a flask, normal calcium phosphate is precipitated; urine which is fully acid within the normal range may be boiled without any such precipitation occurring. To account for the phenomenon various hypothetical explanations have been proposed, many of a very complex kind. The various explanations advanced may be summed up, according to Halliburton ('Text-book of Chemical Physiology'), by saying that the precipitation is the result of unstable equilibrium among certain phosphates, the balance of solubility being easily disturbed by changes of temperature and reaction, and probably modified by the kind and amount of other salts in solution, of which explanation it is sufficient criticism to say that it shows there is none.

Now I venture to submit what I believe is the correct explanation, one that admits of direct demonstration, and one that has not yet been, so far as I know, suggested.

This, then, is the explanation. The boiling brings about the hydrolysis of the urea in the same way that this is brought about by the proper process of fermentation, and it is the continuous evolution of ammonia that leads to the precipitation of normal calcium phosphate. It is of course well known that if solid urea be heated on platinum-foil, it melts and gives off ammonia; the substance which remains is biuret; when biuret is heated it gives off ammonia, and cyanuric acid is left. But what I am able to show is that urea in solution will undergo the same change at the boiling temperature, and even below it.

Acid urine may be freely boiled without any precipitation of normal calcium phosphate taking place. But if, after having been boiled, the simple expedient be adopted of lightly securing a cap of cotton wool over the mouth of the test-tube, and the boiling be then resumed, the urine will in many cases rapidly grow turbid from the precipitation of what microscopic examination shows to be amorphous phosphate.

The same experiment can be made more strikingly with a flask of acid urine.

Now the explanation is that the escape of ammonia, which I will presently show to occur, is hindered by the capping of the vessel, and ammonia being retained in the fluid reduces the acidity to the point required to bring about the precipitation of normal calcium phosphate; the acid phosphate of lime is reduced to the normal. If, however, urine is but slightly acid, or neutral,

or alkaline, the amount of ammonia disengaged by boiling in an open test-tube suffices for the precipitation.

But although in acid urine no precipitation is induced on boiling in an uncapped vessel, this is only if the ebullition is not prolonged. If a flask of fully acid urine be boiled sufficiently long the precipitation may in all cases with certainty be effected; the urine becomes first turbid, and as the boiling is further prolonged an abundant white precipitate is thrown down; but the boiling may need to be kept up for a quarter of an hour. In time, therefore, the amount of ammonia evolved by boiling a fully acid urine becomes sufficient to produce the precipitation.

The evolution of ammonia may be proved in two ways; by the reaction of wetted litmus paper to the vapour, and of Nessler's reagent.

If red litmus paper be moistened with distilled water and held in the vapour of boiling acid urine, it acquires immediately a deep blue colour before any turbidity has arisen in the fluid; and the same evolution of ammonia so shown continues indefinitely after an abundant precipitation of phosphates has been brought about: the blue colour disappears completely as the test-paper dries. The reaction of the boiling urine itself is not always the same. If blue paper be rapidly dipped into the boiling fluid when turbid it may be instantly reddened, whilst the vapour is alkaline from the presence of ammonia.

If a rod of white glass, of which the end has been dipped in Nessler's reagent, be held in the mouth of a flask or test-tube of boiling acid urine, the brown discoloration characterising the presence of ammonia is at once obtained, and this whilst the boiling fluid is still quite clear. The evolution from acid urine increases until the precipitation of the phosphates occurs.

Experiment.—Fully acid urine just voided, which gave a strong red colour to blue litmus paper and no blue colour to red, was boiled in an open flask. Whilst still clear, and after boiling five minutes, the vapour gave the ammonia reaction to Nessler's reagent and to red litmus paper; after boiling for fifteen minutes it was still clear, but the reaction of the vapour with Nessler's reagent was highly pronounced: very shortly afterwards the urine grew turbid from phosphatic precipitation.

That this continuous evolution of ammonia from boiling urine is due to the hydrolysis of its urea is confirmed by the fact that

a similar result attends the boiling of solutions of pure urea. If a solution of urea in distilled water be prepared of the standard urinary strength, 33 grammes to 1½ litres, and boiled in an open flask, the ammonia reactions are most easily obtained in the vapour within a short space of time.

The precipitation of phosphates in urine by boiling may be repeated over and over again if the precipitate be periodically removed by filtration.

Experiment.—I capped with cotton wool a flask of acid urine, and boiled till phosphatic precipitation occurred. Twenty-four hours afterwards, the cap being kept on, the fluid was quite clear, the precipitate having subsided; the fluid gave the litmus paper an alkaline reaction, which gave place to an acid reaction as it dried, proving the alkalinity to be due to ammonia. I then filtered the urine of its precipitate and again boiled it, after capping the flask; a second abundant precipitation of phosphates occurred. Twenty-four hours later the urine was quite clear with a phosphatic sediment, and red litmus paper gave with the fluid a good blue colour, which disappeared on drying. Again filtered, and boiled for half an hour, it grew turbid very quickly. Forty-eight hours later there was no amorphous precipitate, but instead, sparsely scattered over the bottom of the vessel, gigantic house-top crystals; to red paper the fluid was alkaline, the blue colour passing away on drying. I filtered, and on again boiling a precipitate was thrown down of what microscopic examination showed to be amorphous phosphate and house-top crystals of ammonio-magnesian phosphate of the usual size. Twenty hours later I again filtered, and again on boiling the clear filtrate it grew turbid before ebullition was actually reached. Throughout the experiment the flask was capped with cotton wool.

The explanation of such a repeated precipitation doubtless is that the disengagement of ammonia reduces to the normal state only a certain portion of the acid phosphate of lime; when the precipitate is filtered off, and the boiling repeated, a further portion is reduced, and so on.

From urine, except that which gives a highly acid reaction, a minute quantity of ammonia is disengaged immediately after its voidance.

This may be shown if urine be passed into a flask, and immediately a rod of white glass, the end of which has been dipped in

Nessler's reagent, be inserted above the urine, the flask being tilted on its side and the ammonia retained in the air within the flask by having the rod passed through a tightly fitting plug of cotton wool; the rod should be kept gently twisted, when a pale yellow colour will soon appear.[1]

Is it that the urea is hydrolysed at the body temperature? Were it so, the disengagement of ammonia should be continuous if this temperature is maintained. As a fact, I have kept a flask of urine, sterilised discontinuously at 60° C. for four successive days, for eight weeks in the incubator at 35° C., without any phosphatic deposition taking place, although the flask was closely capped, and this notwithstanding that it was amphoteric before incubation. But a temperature of 60° C. will cause hydrolysis in a small degree. Fully acid urine after sterilisation at 60° C. for four successive days commonly becomes amphoteric; and urine that is amphoteric when passed may in the same space of time grow turbid, and deposit a thin white sediment of normal calcium phosphate.

I am not prepared to say that no hydrolysis whatever occurs at the body temperature. I believe it may, for in the atmosphere above

[1] It is absolutely necessary for these experiments that the Nessler's reagent should be as sensitive as possible, and I am indebted to Mr. C. G. Stewart, Chemical Assistant at the Medical School of St. Thomas's, for the following note on its preparation.

Nessler's test.—Dissolve 50 grammes of iodide of potassium in a small quantity of distilled water, heat to near boiling, and add, drop by drop, a saturated solution of mercuric chloride, with constant stirring, till the scarlet precipitate of mercuric iodide just ceases to redissolve. In another vessel dissolve 150 grammes of caustic soda, or 200 grammes of caustic potash, in as little water as possible; add this to the first solution and mix thoroughly. Make up the volume with distilled water to nearly one litre.

This is ordinary Nessler test, and is deficient in sensitiveness for delicate experiments.

To sensitise, add cautiously, drop by drop, a saturated solution of mercuric chloride with constant agitation, till the brown precipitate, which at first redissolves, just begins to be permanent. Allow to settle, and pour off the clear liquid into a small bottle for use as required. It should be of a pale brown colour and perfectly clear. Ammoniacal vapours must be kept out of its way, and an india-rubber stopper is better than a glass one, as the latter is apt to stick. 2 c.c. added to 50 c c. of pure ammonia-free water should give a distinct brown tint with 1 c.c. of a solution containing $\frac{1}{1000}$ of a milligramme of ammonia.

solutions of pure urea that have been kept stoppered for considerable periods the presence of free ammonia is readily discoverable by inserting a rod of white glass dipped in Nessler's reagent into the vessel.*

The presence of free ammonia in urine is the explanation, I submit, of the curious reaction to litmus paper that urine often presents. The acidity of the urine varies much during the twenty-four hours. Fully acid urine offers nothing paradoxical. But urine that gives only a faint red colour to blue litmus paper will give also a faint blue colour to red; it is both slightly acid and slightly alkaline at the same time, or, as it is termed, amphoteric. Now in the case of urine this amphoteric reaction is due to the presence of free ammonia; for if the test-paper be allowed to dry, it will be seen in all cases that the blue coloration entirely disappears from the red paper, whilst the red colour becomes intensified in the blue.

Urine, indeed, in the last stage of ammoniacal fermentation is alkaline only from the presence of free ammonia; for if the red litmus paper that is turned blue be allowed to dry the blue colour disappears; and blue paper wetted with ammoniacal urine becomes as the ammonia escapes red, and when quite dry this colour is highly pronounced, showing that, apart from the free ammonia present, the fluid is acid.

If the reaction of amphoteric urine which is allowed to decompose in an exposed vessel be taken daily, the double reaction will be given after the fluid has begun to grow turbid and deposit normal calcium phosphate; it becomes less and less acid, and when the house-top crystals of ammonio-magnesium phosphate form the amphoteric reaction gives place to an alkaline, though, as before observed, the wetted blue paper soon acquires a red colour as the ammonia is lost on drying.

In passing, the reaction of fresh milk, as is well known, is also amphoteric. But here it will be found that the alkaline reaction persists on drying the test-paper; hence it is clear that the alkalinity is not due to the same cause as that of urine.

Possibly it is the disengagement of the free ammonia that leads sometimes in acid urine to the subsequent deposition of uric acid in the crystalline form—the so-called acid fermentation; but of this I have no proofs.

* A similar disengagement of ammonia takes place from solutions of nitrate, sulphate, or oxalate of ammonia, which become in time consequently acid.

Finally, to complete the proof, a precipitation of phosphates similar to that occasioned by boiling may be induced synthetically.

If solution of ammonia be added in excess to acid urine in the cold, a beautiful crystalline deposit is immediately thrown down of ammonio-magnesium phosphate, which microscopic examination shows to be almost exclusively of the "feather" form, although amorphous calcium phosphate occurs as well, together with a few house-tops of the triple phosphate. To determine whether amorphous calcium phosphate could be artificially precipitated as it is in boiling urine, I imitated the process in detail. If acid urine be boiled in a test-tube and whilst still clear the end of a glass rod previously dipped in ammonia solution be plunged in, turbidity immediately arises, and on allowing the precipitate to settle I found it to consist microscopically solely of amorphous phosphate; on the addition of a few drops of hydrochloric acid the urine became again clear.

The natural result was thus completely reproduced; and on immersing blue litmus paper into the hot fluid an acid reaction was given, although the precipitation had taken place; in this, again, repeating what holds in the other case.

It is, in short, the amount of ammonia that makes the difference in result, whether only amorphous calcium phosphate be thrown down, or ammonio-magnesium phosphate in conjunction with it. This can be shown as follows:—If a drop of acid urine on a slide be placed beneath a watch-glass to the inner surface of which is stuck a piece of filter-paper moistened with ammonia solution, the vapour will effect a speedy deposition in the urine, chiefly of feathered ammonio-magnesium phosphate; if, however, the filter-paper hold but a trace of ammonia, the drop of urine will become turbid as in the first case, but the turbidity will be seen on microscopic examination to consist almost entirely of amorphous calcium phosphate, with scarcely any feather forms of the triple phosphate. And so it is in the process of ammoniacal fermentation; amorphous calcium phosphate is first deposited, and as the ammonia increases in amount the crystalline phosphate of ammonium and magnesium.

The action of Proteus vulgaris *and* Pyococci *on normal human urine.*

After this preliminary digression I may proceed with the more immediate subject of the inquiry.

By the isolation of micro-organisms from ammoniacal urine, as before stated, certain forms are found which will effect the hydrolysis of urea in urine which at the outset is acid. And in text-books of surgery there is thence deduced the statement that whenever urine is found ammoniacal during life, the change is due to the action of one or other of these organisms, *e. g.* the bacterium or the micrococcus ureæ.

What I have been interested for some time past to inquire experimentally was this, whether such a change could be induced in normal urine by pure cultures of the microbes of such supreme importance in surgery as those which cause suppuration and putrefaction.

I selected, therefore, the common organism of putrefaction, *Proteus vulgaris;* and *Pyococcus aureus, Pyococcus albus,* and *Streptococcus pyogenes.* Will all or any of these set up ammoniacal fermentation? The bearing of the results may be discussed at the conclusion of the paper.

Method of experiment.—The urine used was in all cases when passed acid, and not amphoteric. It was filtered to free it of what little mucus it contained into flasks which had been previously plugged with cotton wool and had been sterilised for an hour at 150° C. in the hot-air steriliser. The flasks of urine were then sterilised at 60° C. on four successive days. When a bulk of fluid is to be sterilised, I have never trusted to a single hour's sojourn in the steriliser; usually three hours or longer have been the daily period allowed.

Urine so sterilised will keep unchanged for an indefinite length of time. But in most cases urine that is acid and not amphoteric when passed becomes amphoteric by this process of sterilisation at 60° C. It may be tested from the flasks by inserting the platinum loop after sterilisation in the flame, and then applying it to litmus paper.

For inoculating the sterilised urine I used a platinum wire made into a loop of larger size than usual, and bent into a sort of

gridiron, so as to more fully infect the fluid. After inoculation the cotton-wool plugs of the flasks or tubes were singed and replaced, wetted with sublimate solution, and tightly covered with caoutchouc caps; they were then transferred to the incubator, and kept continuously at 35° C.

The cultures used were specially carried on a few days previously to broth or gelatin, and incubated at 35° C.

Proteus vulgaris.

Of this organism I have obtained pure cultures very readily as follows:—Portion of fresh muscle is minced and placed in a small glass jar with a ground top, the jar being partly filled with distilled water, covered, and then placed in the incubator. As soon as a zooglœa appears at the surface a broth tube is inoculated from the zooglœa and incubated. After twenty-four hours, from the broth tube, now turbid with growth, a second tube of broth is inoculated (or a tube of sterilised salt solution), and from this second tube, after agitation to distribute the organisms transferred, a tube of liquefied jelly, 10 per cent., is inoculated and poured out into a sterilised capsule. In about forty-eight hours the solid jelly is studded with white points, each at the bottom of a deep circular pit of liquefied and slightly turbid jelly. Some of the colonies lie quite below the surface, and such appear as spheres of slightly turbid fluid jelly with central white spot, not unlike frog's spawn. From the separate colonies the organism may be carried on to tubes of agar or jelly.

In stich cultures on glycerine agar, incubated at 35° C., after twenty-four hours a line of growth ranging from between 2 and 3 mm. in breadth is to be observed; the growth is moist, somewhat white, of fair thickness, opaque, with slightly wavy borders; the furrow in the depth of the agar is filled with similar growth.

The growth, which preserves its characters throughout, extends over the face of the medium, but this is only slowly, though the culture be kept at 35° C.; doubtless because the migration of the organism cannot take place on the solid medium.

After sixteen days, for instance, the culture will have an average breadth of only 3 mm.; no extension whatever occurs at any time from the growth in the furrow into the depth of the agar.

Narrow extensions from the lower and broader part of the

culture may then grow up by the sides of the tube, a well-known occurrence in many instances; and these commence to coalesce with the central from below (twenty-four days), though even at this period the upper narrower end of the central streak may be but 5 mm. in breadth. The edge of the streak appears as a thinner and less opaque band with slightly undulatory margin and regularly plaited in low folds, the markings of which lie at right angles to the long axis of the streak. Even after forty-two days, when the agar has commenced to dry, an uncovered strip of the medium will remain on either side of the central growth between this and the extension at the sides.

The macroscopic characters presented by growths in gelatin are well known from the commonly cited description of Hauser. These, however, are such as are observed only in a 5 per cent. medium, and I may notice in a word or two the appearances observable in the medium more commonly in use, viz. 10 per cent.

Characters of stich cultures in 10 per cent. nutrient gelatin:—In tubes kept at the ordinary room temperature, after twenty-four hours extensive liquefaction has occurred in the course of the needle track, the fluid jelly flowing to the bottom of the space in the tube, and laying bare a deep and rapidly widening furrow. In the accumulating fluid, and even after the whole of the jelly has liquefied, three zones may always be detected. The chief portion of the growth settles at the lowest part as a loose white heap-cloud; above this is a zone of fluid jelly almost clear, though holding in suspension a certain number of fine granules; this comparatively clear zone merges above into a third that is turbid.

Characters in stich cultures in nutrient gelatin, 10 per cent.:—After twenty-four hours liquefaction has occurred along the greater part of the needle track, most extensively in the upper part. The fluid jelly is turbid, but it is sharply defined; there is no extension of the growth in any form at the sides into the surrounding solid portion of the medium. In the centre of the liquefied column is an opaque, white, loose, somewhat coarsely granular, crumbling growth.

In the lowest part of the needle track may be a few discrete colonies, around which no liquefaction has yet occurred; such, when present, are spheroidal, isolated or aggregated in small groups, translucent, whitish, quite sharply defined, though from some a lens may show very fine, short, hair-like processes. Around

such colonies liquefaction of the jelly in the immediate neighbourhood ensues, the liquefied jelly becoming turbid whilst the colonies themselves remain amidst the fluid as opaque white points, which finally lose their individuality, and coalesce into a shapeless, white, opaque, central cloud in the turbid jelly.

Characters of strich cultures in shallow capsules of 10 per cent. nutrient jelly:—In the earliest stages the growth appears along the needle track in slightly raised, minute, semi-transparent, greyish points; these are best observed if the capsule be kept in a refrigerator, so as to retard the growth, under which circumstances colonies of this kind may be observed eighteen and even fifty-six hours after inoculation in spots where a minimal amount of the organism has been sown.

Liquefaction of the jelly rapidly proceeds around the colonies, the liquefied jelly being very slightly or faintly turbid; the foci coalesce into a fluid streak. No migration from the streak over the adjoining surface of the medium takes place in the 10 per cent. jelly. On the fluid and faintly turbid jelly is to be seen a complex system of floating islands of various forms, distinguishable by their greater opacity and whiteness; there is often just within the liquefied area a narrow white line of growth accurately following its limits, and continuous on the inner side with many of the processes which float at the surface of the fluid area of the medium. Sometimes the white zooglœa appear as a floating fenestrated membrane. The liquefying jelly is remarkably viscous and ductile. This is by no means characteristic; it is seen in growths of *Bacillus subtilis*, and other organisms which induce liquefaction.

The above characters persist whilst the liquefaction of the medium progresses. The whole is at length changed into a slightly turbid fluid, on and in which are whitish films and clouds of the most irregular branching forms, associated with numerous smaller points, which, from their smallness, appear to the eye as circular; the odour is very foul.

Finally the colonies lose defined outline, and slowly sink or subside in the fluid.

Action of Proteus vulgaris *on normal urine.*

Out of many experiments, which gave uniformly the same results, I may recount the following:

Experiment 1.—July 18th, 1891. A flask of sterilised urine inoculated.

20th.—There is a moderate amount of finely divided sediment in the lower layers of the fluid, which is otherwise clear.

22nd.—Upper part of urine clear, becoming turbid in the lower, and forming a sediment readily distributed on agitation. At the level of the top of the fluid there adheres to the inside of the flask a narrow stippled deposit.

24th.—No obvious increase of growth. A fine sediment over the bottom of the flask, not completely covering it. No crystals. Fluid generally clear.

31st.—Nessler's reagent introduced on a rod and held above the fluid gives no ammonia reaction.

August 6th.—A fine sediment of the growth in irregular islands, the greater part of the bottom of the flask being uncovered. No crystals. The narrow white rim on the vessel at the level of the top of the fluid remains. Reaction amphoteric.

22nd.—Same report.

September 15th.—Same report.

20th.—Same report. Reaction amphoteric.

October 30th.—A thin white deposit at bottom and sides of the vessel; two large feather crystals. Reaction alkaline.

Exp. 3.—July 29th, 1891. A test-tube of acid urine, sterilised as previously described, was inoculated with the öse.

30th, one day. Uniformly distributed, but not marked, turbidity; with a lens a fine particulate suspension is visible; no sediment, no zooglœa.

Two days. Same report.

Five days. Slight general turbidity persists. There is a thin sediment over the bottom of the tube, detachable by agitation.

Eight days. A loose, thin, whitish deposit at bottom of the tube, invisible on shaking.

Twelve days. Faint general turbidity. There is in suspension a moderate amount of loose flocculent growth and a sediment of similar kind.

Nessler's reagent on the white rod introduced above the fluid gives

no reaction indicating free ammonia. To litmus paper, a drop of the urine withdrawn on the öse gives red reaction to blue paper, but no blue to red paper, the fluid being still acid and not amphoteric.

Fourteen days. Same report. An incomplete narrow whitish line of deposit adheres to the inside of the tube at the level of the top of the fluid. No free ammonia in the air of the tube.

Twenty-four days. No general turbidity. Loose flocculent growth in suspension in certain parts of the fluid, and as a sediment; white rim as before.

Thirty-two days. Reaction amphoteric.

Fifty-three days. Reaction amphoteric, general characters as before. No crystals.

Ninety-three days (October 30th, 1891). Amphoteric. No crystals.

Exp. 7.—October 30th, 1891, a flask of urine inoculated. Reaction when passed acid. Reaction after discontinuous sterilisation and immediately before experiment amphoteric.

31st.—No change.

November 4th.—Turbidity arising.

5th.—Very thin deposit at the bottom and lower part of sides, white and fine on displacement by agitation.

20th.—The sediment is comparatively small.

28th.—No crystals; amphoteric.

December 9th.—Nothing new.

July 1st, 1892.—No crystals. Fluid generally clear; the sides and bottom of the vessel are covered with a thin white film. Reaction alkaline.

Exp. 9.—October 31, 1891, flask of urine, amphoteric immediately before inoculation, infected with *Proteus vulgaris*.

November 2.—Slight deposit at sides and bottom, with a narrow adhering white line at level of the fluid.

5th.—General turbidity; moderate deposit at sides and bottom.

16th.—Nothing new.

28th.—Amphoteric; no crystals.

December 9th.—Nothing new.

July 1st, 1892 (eight months after the inoculation).—Whitish deposit at bottom and sides. Reaction alkaline. Large feather crystals in groups at bottom, and large hedgehog crystals. After washing, the feather crystals proved on testing to be pure ammonio-

magnesium phosphate, the hedgehogs to be common tribasic phosphate.

The whole series of experiments made shows that although *Proteus vulgaris* will grow in amphoteric, and even in acid urine, its growth is slow and of limited extent. And although in its growth the acidity of the urine is reduced, so that acid urine will become amphoteric, the production of ammonia is so insignificant that the micro-organism must be reckoned as having scarcely any hydrolytic action on urea.

The proper nourishing substance of Proteus is proteid; in this the microbe finds its proper sphere of action as truly as Saccharomyces does in sugar, or Bacterium aceti in alcohol. For this reason normal urine is unfitted for its growth, the only constituent allied to proteid being the small amount of mucus which exists in it. The acidity of the fluid alone does not explain the result. If Proteus is sown in Nägele's or Cohn's solution, neither of which is acid, there is but slight multiplication of the organism (Flugge).

Pyococcus aureus; Pyococcus albus.

The cultures used I obtained from the pus of an acute abscess of the bursa patellæ, in which the two micro-organisms occurred together.

The isolation of these organisms by plate culture is to be accomplished only with care, for at their first appearance the colonies of *aureus* are not distinguishable from those of *albus*.

The rate at which the yellow coccus acquires its colour is variable. In strich cultures of the pure organism on agar, inoculated at 35° C., without being capped, the line of growth as it appears after twenty-four hours may be quite devoid of yellow colour. After forty-eight hours the white growth may be of a pale yellow, except at the growing margins, where it may be still white. After seventy-two hours the growth may be of a pronounced yellow colour, paler at the edges. The colour slowly deepens, and in a few days the culture has commonly acquired a brilliant orange or golden yellow. The rate of pigmentation, however, varies much, even in the different generations of pure cultures carried on from the same stock.

It is this which explains the view taken, for instance, by Jaboulay,

Bertoye, Rodet, Lépine, and G. Roux, that the two organisms are identical. Thus Rodet, from observing that the gelatin culture from an abscess was white at first and became a little yellow the following days, whilst a new culture with this gave orange colonies, concluded that *albus* may become transformed into *aureus*.

Lépine and G. Roux, on adding acetanilide (antifebrin) to the nutrient gelatin, have obtained white cultures from yellow, and on then cultivating the unpigmented cultures on pure gelatin these have again returned to yellow.

In my experience, after having had these micro-organisms under observation for a long period, whilst certain cultures of *aureus* may evince little pigmentation, and a complete colouration of the whole culture may be long delayed, the generations of a pure culture of *albus* remain throughout devoid of colour.

To show that *aureus* may fail to produce pigment is not sufficient to establish identity; *Bacterium prodigiosum* not infrequently does the same when grown on agar or gelatin. It must be shown that there are no unpigmented cultures of Pyococcus which cannot be made to produce the yellow colour, and only such, of course, should be designated *Pyococcus albus*.

Action of Pyococcus aureus *and* albus *on urine.*

From cultures of these micro-organisms recently carried on in nutrient gelatin at 35° C., I inoculated a series of flasks and test-tubes of urine discontinuously sterilised at 60° C.; they were kept at 35° C. closely capped.

The uniform result of seven experiments is to show that *aureus* produces rapid and highly pronounced ammoniacal fermentation; *albus* is equally effective. The urine inoculated, although acid when passed, became in most cases amphoteric as a result of four days' discontinuous sterilisation. In one instance, however, it remained acid. The reaction was tested with the öse immediately before each experiment. In the acid urine the fermentation was even more rapid than in some of the amphoteric samples.

The notes of the case referred to are as follows:

Exp. 6.—October 30th, 1891, a test-tube of urine discontinuously sterilised, and *acid* immediately before the experiment, was inoculated with *Pyococcus aureus*.

31st.—Slight deposit at sides and bottom.

November 1st.—Fine deposit over sides.

2nd.—Several beautiful feather crystals of triple phosphate adhere to the sides, some more than ·5 cm. in length.

7th.—Crystals more numerous. They are larger in size than in a tube of amphoteric urine inoculated the same day, though their numbers and the amount of phosphatic deposit are about the same in both.

28th.—Reaction, as shown by dipping in the öse and applying it to test-paper, strongly alkaline, and, as told by the appearance of the red colour on blue paper after standing, due to ammonia.

July 26th, 1892.—Same report *in toto.*

Exp. 7.—October 30th, 1891, a test-tube of discontinuously sterilised urine, amphoteric before the experiment, though acid when first passed, inoculated with *Pyococcus aureus.*

November 1st.—Deposit on one side of tube and at bottom.

2nd.—White deposit at bottom and slightly at sides. Well-formed feather crystals of triple phosphate lie in the amorphous deposit at the bottom of the tube.

5th.—Crystals increased in number.

28th.—Reaction strongly alkaline.

July 26th, 1892.—Same report *in toto.*

Exp. 5.—October 30th, 1891, a flask of amphoteric urine inoculated with *Pyococcus aureus.*

October 31st.—Abundant white precipitate on sides and bottom of flask. Fluid generally turbid.

November 2nd.—No crystals.

5th.—In the abundant, white, amorphous deposit there have appeared numerous bright house-top crystals sticking to the sides of the flask.

16th.—The deposit is now very dense; crystals not increased in size.

28th.—Reaction strongly alkaline.

July 26th, 1892.—Same report. Strongly ammoniacal to smell. The crystals, which thickly cover the bottom and sides, are shown on testing to be ammonio-magnesium phosphate. The white deposit shaken in a test-tube of distilled water dissolves on the addition of hydrochloric acid.

Exp. 1.—July 18th, 1891, a flask of discontinuously sterilised urine inoculated with *Pyococcus aureus.*

20th.—Urine turbid throughout, with an abundant sediment.

24th.—Same report.

28th.—Besides the abundant deposit of white amorphous phosphate, huge feather crystals of triple phosphate have formed.

31st.—A white glass rod dipped in Nessler's reagent and held in the flask above the fluid gives an immediate and marked brown coloration, indicating the presence of free ammonia.

Exp. 2.—July 22nd, 1891, a flask of discontinuously sterilised urine inoculated with *Pyococcus aureus*, and another flask with *Pyococcus albus*.

24th.—There is in each flask an abundant white deposit at the bottom, and a thin layer adhering to the sides of the vessel. Urine generally turbid.

28th.—Same characters, but in the sediment and adhering to the sides of the flasks are gigantic feather crystals of ammonio-magnesium phosphate.

The experiments cited will be sufficient.

Within twenty-four hours after inoculation a deposition of white amorphous phosphate is to be observed, which continues to increase for a few days in amount, and this is soon followed by the formation of crystals of ammonio-magnesium phosphate. In one instance I have seen crystallisation occur within forty-eight hours after inoculation; in only one case was it delayed beyond seven days.

Streptococcus pyogenes bovis: *its action on urine.*

For the original culture of this micro-organism I am indebted to Professor Crookshank.

The growth of this organism in urine occurs very slowly, and although it may eventually lead to the precipitation of amorphous phosphate, and even to the formation of crystals of ammonio-magnesium phosphate, these occur to such limited extent, and the crystallisation only after so long a period, that for clinical purposes it may be disregarded as an agent inducing ammoniacal fermentation.

In the last of the four experiments made the urine immediately before inoculation was amphoteric, and it was almost certainly so in the first and second, since it is altogether exceptional for urine to remain acid without becoming amphoteric after discontinuous sterilisation at 60° C. for four successive days.

Exp. 1.—July 18th, 1891, flask inoculated.

20th.—Fluid slightly turbid throughout, with a certain amount of deposit.

22nd.—Same report. The deposit is readily miscible on agitation.

28th.—The fine sediment does not by any means cover the bottom of the flask.

31st.—Same report. On testing the air within the flask by a white rod dipped in Nessler's reagent no trace of free ammonia was shown.

August 7th.—Still faint general turbidity, and a fine sediment in irregular islands, the greater part of the bottom of the flask being uncovered by the deposit. Reaction amphoteric.

October 30th.—No crystals. Reaction amphoteric.

Exp. 3.—July 29th, 1891, test-tube of sterilised urine inoculated.

31st.—General turbidity, with a slight sediment.

August 3rd.—Same report.

6th.—Slight general turbidity; a small amount of sediment at the centre of the bottom of the tube.

12th.—Same report.

22nd.—General turbidity gone. The growth is in coarse, loose, flocculent grains in suspension and at bottom of tube. No crystals.

September 20th.—Nothing new. No crystals. Reaction acid, not amphoteric. (This urine was therefore acid before the experiment.)

October 30th.—No crystals.

Exp. 4.—October 31st, 1891, flask of urine amphoteric immediately before inoculation.

November 1st.—General turbidity; thin deposit at bottom and sides.

7th.—Deposit at bottom is in patches parted by wide gaps, and covering only a small part of the bottom of the flask.

16th.—Fluid still turbid generally.

28th.—A fair deposit of white amorphous phosphate coating the sides and bottom of the flask. Reaction amphoteric.

Streptococcus pyogenes hominis.

August 3rd, 1891, a flask of urine inoculated from a recent broth culture.

4th.—No change.

6th.—No change.

10th.—No change. Flask re-inoculated.

12th.—No change visible.

22nd.—Fluid clear. There is a coarsely granular white growth in lumps, not in any quantity.

30th.—Same report. No crystals.

September 7th.—Lying at the bottom of the flask of the perfectly clear urine are irregular groups of whitish growth in coarse cohering grains.

20th.—Same report. Amphoteric.

October 30th.—Same report. Amphoteric.

Concluding remarks.

The ammoniacal fermentation of urine has been hitherto assumed to arise only through the direct transference from without of *Bact.* or *Micr. ureæ*, by the use of catheters or otherwise. When this fermentation takes place in cases where no catheterisation has been resorted to, the theory proposed by writers on scientific surgery is that the microbial infection extends directly from without, through the medium of the ropy mucus which lines and clings to the urethra, the hypersecretion itself being due to the cystitis which results from or is associated, say, with a stricture of the urethra.

From the demonstration that Pyococci will induce ammoniacal fermentation it must be concluded that this change may arise altogether apart from the direct introduction of microbes from without. The suppurative process would itself suffice for it.

Hence, for example, a suppurative pyelitis[1] confined to the kidney might be in itself sufficient to lead not only to a simple chemical deposition of normal calcium phosphate by reason of a heightened local alkalinity due to an increase of mucus and the addition of inflammatory exudation to the urine, but to bring about fermentation, and lead, in addition, to the formation of crystalline phosphate of ammonium and magnesium: it is commonly assumed that when ammoniacal fermentation of urine is found within the renal pelvis, this is always due to an extension of the causes leading to fermentation from the lower part of the urinary tract.

[1] The purely tubercular form is not considered, as its pathology is altogether different.

Where infection from without is in question many considerations need to be dealt with. In the first place, the introduction of Pyococci in catheterisation will give rise to fermentation, as well as the introduction of *Bact.* or *Micr. ureæ*. *Proteus vulgaris* would have no result.

But in one or other way, or probably most often in all, ammoniacal fermentation is set up. Here, again, exception may be taken to the common statements in regard to the consequences of this. It might be gathered from the ordinary statements that ammoniacal fermentation, as such, in itself was fraught with danger. All the dire results that may follow this are ascribed to it. It is hardly conceivable that the mere formation of ammonium carbonate in itself would lead to the consequences referred to.

Now the true importance of ammoniacal fermentation lies in this, that it is an index of other and more important changes which are from the first or secondarily associated with it—to wit, putrefaction and suppuration; and it is upon these that the evils really depend.

Normal urine is a medium in which *Proteus vulgaris* will hardly grow; there is practically in normal urine no proteid from which toxines are producible.

But with urine occupying inflamed cavities the case is widely different. It is then that proteid is added in the inflammatory exudation poured from the vessels of the mucous membrane, and then that the urine may become, if infected with putrefactive organisms, putrid as well as ammoniacal; and the resulting evils admit of explanation on the general principles established in regard to putrefaction when free drainage is not secured.

Among the products of such proteid decomposition ammonia would be one, but, needless to say, it is not to this that the evil is to be attributed, any more than to the ammonia produced by the simultaneous introduction of *Mic.* or *Bact. ureæ*, but to the proteid toxines and toxic alkaloids elaborated through the agency of the putrefactive organisms.

In some cases, before catheterisation is had recourse to, the urine already contains proteid from the catarrhal condition of the urinary passages. And as the infection from without, supposing it to occur, will be a mixed one, there will be set up in such urine putrefaction of proteid, together with ammoniacal fermentation of urea; the antecedent inflammation will be enhanced, the proteid thereby increased in amount, and its decomposition will further increase

the inflammation. And finally the process of suppuration adds a yet further complication; for in the case supposed a direct introduction of pyogenic organisms would probably take place with the others, and these would add to the proteid toxines formed by the putrefaction.

Lastly, the subject of indirect infection may be referred to, *i. e.* infection through the blood-stream, when the blood in conditions of lowered health may be unable to destroy the pyogenic microbes reaching it, and when thus a simple inflammation may be converted into one that is infective.

In this way, as before noticed, a simple catarrhal pyelitis set up by a calculus might become suppurative, a catarrhal cystitis purulent, and in both cases ammoniacal fermentation might be brought about apart from any infection introduced directly from without.

In the same way, under certain conditions of ill-health, an extravasation of normal urine in a closed space might become ammoniacal. As hæmatomas may now and then excite suppuration, so may extravasations of normal urine, and in the latter case the action of the Pyococci will bring about ammoniacal fermentation; it is this that renders it unwarrantable to assert that such an extravasation within a closed space will never undergo ammoniacal fermentation. Not only may the general condition before the accident be such as to bring this about by leading to an indirect infection, but an equally effective general condition might result from the accident itself.

In the case of extravasation following on stricture of the urethra the same methods of indirect infection may obtain, though in most of the non-traumatic cases, at least, the urine would hold proteids and be probably foul before the extravasation occurred, or if not infected, that extravasated would stand the chance of becoming so through the medium of the peri-urethral abscess which often precedes the urethral rupture.

The fact that Pyococci suffice to set up rapid ammoniacal fermentation explains, I believe, what in surgery has so long been without an explanation, viz. the decomposition which ensues after fracture of the spine in cases where no instruments have been used. The cystitis that arises under such circumstances is due to the same causes that lead to the inflammation of the integument.

In the case of the skin the ordinary pressure of decubitus

suffices, in consequence of the altered innervation of the parts, to bring about inflammation which may proceed to sloughing; and so in the bladder the distension of the organ brings about an inflammation of the mucous membrane which may be followed by its ulceration and necrosis; the cystitis so set up becomes indirectly infective, and the presence of pyococci in the urine induces ammoniacal fermentation. *November 3rd*, 1891.

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7. *On the inadequacy of the current terms applied to suppuration, with a proposal; and a note on the presence of peptone in pus.*

By Samuel G. Shattock.

When one proposes to offer a new term for what has already a name it must be shown, firstly, that the state of the case requires it; and secondly, that the subject involved is one of sufficient importance to render such a change expedient.

In the case of suppuration both these propositions hold true, and the time has, I submit, come for some revision of the terms in current use, partly in order that the modern truths concerning suppuration may be scientifically expressed, partly because the terms at present used, and which have reached us from a previous generation, do, so far as words can, hinder the general recognition of the true pathology of what is of the highest practical importance.

The terms now employed in relation to this subject, viz. "pus" and "suppuration," are purely anatomical. Perhaps no two processes in pathology are more widely different than those of acute and chronic suppuration in their typical forms, yet they are designated by the same term, *suppuration*, and the contents of the acute and chronic abscess by the same word, *pus*.

It is only so long as a knowledge of ætiology is wanting that the inclusion of different pathological conditions under the same anatomical terms is justifiable; there is, indeed, no alternative.

Setting aside any wider question, that which clinically presents itself as acute suppuration does admit of being distinctly marked

off in its ætiology from other forms of pus formation, and it is to this that the present remarks are limited.

Acute suppuration is a specific inflammation. The terms "common" and "specific" are merely relative. Tuberculosis is "specific," suppuration is "common," or rather it was, for the Listerian principles of asepsis have rendered suppuration, at least that due to direct infection, as uncommon now as it was before common.

Henceforth suppuration must both clinically and pathologically be viewed as a specific form of inflammation, and not the common.

The specific character of the acute inflammation that terminates in suppuration admits of the same exact demonstration as does, for instance, that of tuberculosis; it is superfluous to say that Koch's four postulates may be all satisfactorily fulfilled: (1) the microbes may be shown in the pus of the acute abscess; (2) they may be cultivated outside the body; (3) the specific process of acute suppuration may be induced by the subcutaneous injection, &c., of pure cultures; and (4) in the abscess so produced the same organisms may be demonstrated.

The check experiments are at first a little ambiguous, but they do not affect the main contention, which is the need of some modification in the existing nomenclature.

These experiments, made to determine whether the subcutaneous introduction of chemical substances will produce suppuration, are, as is well known, not uniform in result, even when carried out with the proper experimental precautions. Chemical irritants introduced beneath the skin in capsules, and subsequently let out into the tissues, excite, of course, acute inflammation, but sometimes pus is formed, at others not, though the inflammation may be in both cases simple or non-infective.

In the human subject it is on the clearest clinical evidence that simple injuries, a bruise or a fracture, at times, though very rarely, suppurate—and this, as shown by experiment in the lower animals, owing to the indirect infection of the injured part with pyogenic cocci which reach it through the blood-stream; and so, if animals out of condition be used for such experiments, an infective suppuration may ensue at the site of what at first was a simple inflammation.

But setting this possible fallacy aside, suppuration may be set up experimentally by the subcutaneous introduction of the filtered or chemical products not only of pyogenic cocci, but of *Proteus*

vulgaris, and, again, of certain of the isolated toxic alkaloids formed by the latter. Such substances as these, however, never occur under natural circumstances, except in conjunction with the specific microbes which elaborate them; and, what is more important, the suppuration so artificially induced is different in its history from that which arises as a natural process, for it is non-infective, there can be no addition made to the proteid toxines or toxic alkaloids introduced, and no succession of a secondary set of similar lesions.

But amongst chemical substances in the formation of which micro-organisms are in no way concerned, certain will produce suppuration. The different statements made on this subject appear to be reconciled by the fact that different animals respond differently to the same substance: *e. g.* a solution of 5 per cent. nitrate of silver causes suppuration in dogs, but not in rabbits; turpentine and croton oil cause suppuration in carnivora, rarely in rabbits. In all these cases there is pus formation in the anatomical sense; ætiologically the process is different, for the inflammation, though it terminates in suppuration, is non-infective.[1]

Viewed in its entirety, the process of true suppuration corresponds with that of tuberculosis; and it demands a term which will indicate its specific character, include its secondary manifestations, give a unity to the whole, and mark it as a disease.

The following scheme will serve to show at a glance the similarity referred to between the two processes, though other infective granulomata than tuberculosis would do equally well.

TUBERCULOSIS.

1. Local (tuberculosis). 2. Glandular (tuberculosis). 3. General (tuberculosis).

PYOSIS.

(The process of acute infective or microbial suppuration due to specific micrococci.)

1. Local (pyosis).	2. Glandular (pyosis).	3. General (pyosis).
Acute circumscribed abscess and diffuse suppuration.	Secondary glandular abscess.	Pyæmia.

[1] A similar distinction may be drawn out in other cases. The false membranes which are met with in the trachea from the inhalation of the fumes of strong irritants, like ammonia or hydrochloric or nitric acid anatomically resemble those that result from the poisonous action of the diphtheria bacillus, though they are ætiologically the results of non-specific and simple processes of necrosis and inflammation.

Corresponding firstly with the localised tubercular lesion is the acute abscess, an infective inflammation tending in all cases by its very nature to spread but in most terminating in cure.

The circumscription of an acute abscess is not in any way part of the infective process; this tends indefinitely to spread, but is due solely to the successful resistance offered by the tissues, whether fluid or solid, amidst which the virus is located. As in the history of tuberculosis so in that of acute suppuration, the process may result from direct infection, as witnessed in a furuncle or a wound, or from indirect, as in a case of acute epiphysitis or acute necrosis.

If an instance of acute epiphysitis following a trivial injury or arising without injury at all, differs from one of epiphysial tuberculosis arising under similar circumstances, it is only in this that the virus in the latter case is the tubercle bacillus, in the other *Pyococcus aureus*, &c.

In the next place, of the secondary infection which results from the primary; in tuberculosis this may affect, firstly, the lymphatic glands in anatomical relation with the original lesion. From this the secondary glandular abscess that may arise in the train of acute suppuration in a distant part in no way differs, and like it, it implies the transmission of the virus by the lymph-spaces and lymphatic vessels to the corresponding glands.

If such glandular infection does not always end in the specific way of suppuration it is because the tissues and juices of the gland cope successfully with the microbes; or such inflammation may be due to the passage of the chemical products only from the seat of the primary lesion, which products, owing to the freedom of their passage through the parts, do not accumulate in sufficient quantity to cause suppuration.

Tuberculosis, finally, may become more widely disseminated, either through the blood-stream by way of the lymph, or more directly through the veins involved at the seat of the primary tubercular lesion. And so in the suppurative process the virus may in the same way become disseminated through the veins of the part, and set up inflammation terminating in the same specific manner, viz. suppuration. What general tuberculosis is to the local, pyæmia is to acute suppuration.

What is needed, therefore, is some term so framed as to include the whole of the possible phenomena presented by acute suppura-

tion; and constructing such a one on the same lines as "tuberculosis," that of "pyosis" is one which might be suggested.

"*Pyosis.*"—A specific form of acute inflammation due to specific micrococci, terminating in suppuration, which under favorable circumstances is localised or circumscribed and ends in cure, but which may be followed by secondary glandular infection and glandular abscess, or by a more general infection of the secondary foci of inflammation, terminating, like the primary, in the same specific manner, viz. acute suppuration.

I am well aware that difficulties might be brought forward against such a suggestion. There are difficulties, but they are not different in kind or degree from those which already exist in the case of other specific diseases. They exist even in tuberculosis itself, for there are infective lesions anatomically like those of tubercle which do not depend upon the tubercle bacillus; yet the term tuberculosis is as yet, at any rate, confined to such as arise from the bacillus of Koch.

A note on the presence of peptone in pus.

When to a solution of albumose or peptone a drop of cupric sulphate solution is added, and then excess of a solution of caustic potass, a violet or pink colour immediately appears in the fluid. This, which is known as the biuret reaction, though highly valuable as a test for albumose and peptone, is not characteristic, and is only conclusive when the presence of other proteids is out of the question, or when, by previous methods, other proteids have been removed. This fact is of importance in adopting the reaction as a test for the presence of albumose and peptone in pus, for pus contains other proteids which give it.

If fresh pus is shaken with half its bulk of distilled water and filtered, a drop of copper sulphate solution produces an abundant white precipitate in the slightly turbid filtrate, and on adding excess of caustic potass solution, the fluid, which becomes quite or almost clear, immediately acquires a violet or reddish-violet tint, sometimes of remarkable depth and brilliancy. This is, however, no proof in itself of the presence of albumose and peptone, and is due in part to the other proteids present in pus. Fresh hydrocele fluid or ascitic fluid will give the same reaction.

The presence of peptone in pus I have been able, firstly, to demonstrate by dialysis.

If pus be placed without any kind of dilution in a dialyser suspended in a small beaker of distilled water, the peptone alone of the different proteids present passes through the membrane, and in the water the biuret reaction will show its presence.

But the simplest method of isolating the peptone is by saturation with ammonium sulphate. During the course of last year I tested thirty specimens of pus which were kindly supplied by Mr. E. C. Stabb, the resident assistant surgeon at St. Thomas's Hospital. To the pus in a long test-tube I added half its bulk of saturated solution of ammonium sulphate, and then crystals of the same salt, shaking till a certain number of crystals remained undissolved. The pus is then filtered. The filtrate should be perfectly clear; if it is not, it should be again shaken with a few crystals of ammonium sulphate and again filtered. From the filtrate all proteids are absent except peptone, saturation with ammonium sulphate producing precipitation of every proteid with this exception. The biuret reaction is then got by adding half a drop of copper sulphate solution on a fine glass rod; no precipitate is produced. On now adding excess of caustic potass solution a dense white precipitate of potassium sulphate is thrown down. If peptone be present the white precipitate has a pink tint, owing to the coloration of the fluid in which it is suspended, and on allowing the tube to stand the white precipitate soon subsides, and the supernatant fluid, which is quite clear, will exhibit a pinkish coloration. In this way I tested thirty specimens of typical "laudable" pus, and in all the peptone reaction was obtainable.

The presence of peptone is known to be demonstrable after death in muscular tissue, owing to the fact that the tissues in general contain a certain amount of pepsin; and this, when the reaction of a part becomes acid, is enabled to act upon and convert proteid into peptone.

The reaction of fresh pus, however, is not acid but alkaline, and such an explanation of its containing peptone is thus disposed of; the presence of this body is to be associated, therefore, solely with the action of the pyogenic organisms upon the inflammatory exudation, and whatever portion of the inflamed tissue suffers digestive solution by the action of the same organisms.

For the demonstration of albumose in pus, Dr. Sydney Martin's method is the one I had recourse to, and by means of this the demonstration presents no difficulty. In June, 1891, following

this method, I shook with excess of alcohol, the pus from an acute abscess of the breast and that from a pyæmic abscess of the arm.

The pus was left under alcohol in a stoppered vessel with occasional shaking until January, 1892; it was then filtered, the pale yellow substance left on the filter scraped off and dried at a gentle heat. The dried substance was then well rubbed at intervals for some hours with distilled water in a glass mortar, and left to filter in a refrigerator. The filtrate was a slightly turbid pale yellow fluid.

The alcohol precipitates all the proteids; but of these the albumose and peptone are redissolved with water. The fluid on testing a small quantity gave the biuret reaction. Half the fluid I now shook with crystals of ammonium sulphate to saturation; this produced a white precipitate, in somewhat considerable amount, of albumose; this was filtered, and the clear filtrate gave again the biuret reaction on adding half a drop of copper sulphate solution and excess of solution of caustic potass, showing the presence of peptone.

The formation of albumose and peptone cannot be claimed as peculiar to pyogenic microbes.

Dr. Sydney Martin has shown that on growing anthrax bacillus in alkali albumen, not only is a toxic albumose elaborated, but that traces of peptone may in addition be demonstrated. And I may say, in conclusion, that in all the samples of pus which I have examined the amount of peptone was small; in most cases it amounted only to a trace.

The formation of peptone under all such circumstances is not a little remarkable, for it is clearly of the same nature as that which obtains in the higher carnivorous plants; and it doubtless serves the same end of providing out of proteid material a foodstuff that may be assimilated. Whatever may be the substances produced in cultures which as they accumulate are deleterious to and kill the micro-organism, peptone is certainly not one; for peptone is the common proteid used in the artificial media in which such organisms best thrive, and the fact that it is found at any given time only in small amount points to the inference that what is formed is rapidly made use of by the micro-organism.

Not that proteid is strictly essential to their growth, for pathogenic microbes will grow in such media as Cohn's or Nägele's solutions, though only feebly.

The case, in fact, is precisely as it is in the higher carnivorous plants, which, though they will grow without such food, flourish more vigorously when they obtain it (Sachs, 'Physiology of Plants,' 1882).

In those plants which have been studied (*Nepenthes*, *Dionæa*, *Drosera*) the peptonising ferment of the glands is associated with an acid secretion; in this the process resembles gastric digestion.

In the case of the *carnivorous bacteria*, as those may be called which peptonise proteid, the medium must be alkaline, and in this bacterial digestion is akin to the pancreatic rather than the gastric.

February 2nd, 1892.

XI. DISEASES, ETC., OF THE LOWER ANIMALS.

1. *A litter of five kittens with congenital defects.*

By J. Jackson Clarke, M.B.

The kittens, which were brought to me by Mr. J. Wells of Acton, were all undersized; each one, however, possessed some fully developed parts, so that I have no doubt they were produced at full term. They all presented deformities; thus every one had double harelip and cleft palate. The degree of the latter appeared to be determined by the manner in which the tongue had been pressed upwards; thus in one of the kittens the septum nasi had united to the palate on the left side, whilst on the right side the corresponding border of the tongue was thrust up between the septum and the right half of the palate.

The number and variety of malformations presented by some of the litter was very striking. Mr. J. Griffith kindly prepared for me the lantern slides which were shown at the meeting of the Society. One of these showed the ventral aspect of a kitten and the following defects:

1. Exophthalmos on the right side.
2. Double hare-lip and cleft palate.
3. Diminutive club-hands with but three digits on each.
4. Feet, right with three digits, left with four, affected with marked equino-varus and crossed.
5. Tail stunted and permanently twisted like a corkscrew.

Another photograph showed in the hinder limbs a symmetrical deformity due to great inward rotation and flexion at the knee, with marked pronation of the leg, complete extension of the ankle, and inversion of the foot of such degree that the member formed almost a complete turn of a spiral, the hallux resting on the outer side of the fibula. The condition of the feet corresponded with

most advanced equino-varus, the great length of each segment of the foot permitting the hallux to pass to the outer side of the leg instead of resting as in man against the tibia.

Two of the others had a peculiar deformity of the hinder extremities. On dissection I found the whole of the fibula and the lower half of the tibia absent. This appeared to have been caused by an outward rotation in the leg through an angle of 270°. A rudiment of the os calcis was the only representative of the tarsal bones. One of the metatarsals was absent, and two of the remaining bones were fused together. Several of the kittens had shortened and twisted tails.

I think all the deformities are explicable on the hypothesis that for some reason there existed an abnormal degree of intra-uterine pressure, or, to put it in another way, a considerable limitation of space. In harmony with this explanation is the fact reported to me by Mr. Wells that there is on the left side of the abdomen of the mother a tumour, which was discovered a fortnight after the birth of this malformed litter.

Two litters have been produced since. The first consisted of five full-sized kittens, three of which were talipedic, the second consisted of five full-grown and well-formed kittens. The abdominal tumour meanwhile had remained almost stationary. It may fairly be assumed that the deformities are due to increased intra-abdominal pressure caused by the tumour. It must be further assumed that in some way, perhaps by an increased laxity of the parietes, tolerance has been established. The nature of the tumour can only be ascertained after the death of the mother, which is a family pet. *April 5th*, 1892.

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2. *Diseased feet of ducks, supposed (in South Africa) to be leprous.* (*Card specimen.*)

By P. S. Abraham, M.D.

Not uncommonly in South Africa fowls, pheasants, ducks, &c., exhibiting diseased or deformed extremities, have been considered, even by medical men, to be suffering from leprosy.

These specimens have been in that belief recently sent from the Cape.

Microscopic sections taken from one of them show an inflammatory and carious condition of the bone, but no leprous bacilli or any real evidence of that disease. *November 17th*, 1891.

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3. *A toad whose mouth and nostrils were attacked during life by the larvæ of blow-flies.*

By Leonard Guthrie.

(Introduced by C. B. Lockwood.)

The toad when found seemed in fairly healthy condition, but the tip of the nose was discoloured, the nostrils were slightly enlarged and ragged, and emitted a frothy discharge. Within them could be indistinctly seen a mass of moving larvæ. Within thirty hours of capture the nostrils formed one large cavity, separated only by a thin septum of skin anteriorly; both eyes were collapsed, and their empty tunics lay in the cavity of the mouth, whilst the whole of the soft palate had been devoured by the larvæ, leaving the bones picked bare. Between three and four dozen larvæ were removed after the death of the toad. It was well known that toads and frogs were subject to such ravages, but until the present time no attempt to identify the larvæ had been successful. Dr. T. S. Cobbold had referred to the subject in the 'Veterinarian' for 1880, but had been unable to name the maggots. Prof. Brauer, of Vienna, had kindly examined the larvæ now exhibited, and had pronounced them to be of the genus *Calliphora*. The species was indeterminate, but was probably *erythrocephala*-*magna* or *vomitoria*.

Description of larvæ.—Length $\frac{1}{2}$—$\frac{2}{3}$ in.; shape conical; head pointed; tail much larger than head, and truncated; body divided into twelve segments, including head; between each pair of segments five to ten parallel rows of small pointed scales, directed backward until the sixth segment, when the rows of scales are divided into one anterior set pointing forwards, and two posterior sets pointing backwards.

Mouth cruciform, with four lips, each of which is surmounted by a minute papillæ; four similar papillæ, in two pairs, are seen on the dorsal surface of the extreme end of the tail. The upper pair of lips project beyond the lower.

Masticatory apparatus.—In three portions: (1) hooklets, (2) intermediary portion, (3) body.

Hooklets.—Two, placed parallel, strongly curved downwards; bases square, connected by their inner surfaces, and articulating posteriorly with the anterior surfaces of the intermediary portion. Muscles are attached to the inferior angle of the bases of the hooklets, and serve to protrude, depress, and retract them. In a lower plane than the base of the hooklets are two small, irregularly shaped horny bodies, probably rudimentary lateral maxillæ.

Intermediary portion.—Shaped like letter I horizontally placed; articulates in front with bases of hooklets, behind with anterior portion of the body of the apparatus.

Body of masticatory apparatus.—Shaped like two ploughshares, placed parallel and joined anteriorly. Projecting from anterior surface of it are two long, slender, hamular processes, which perhaps serve to guide the muscles which elevate the hooklets. Only two muscles can be seen: (1) a long strand, passing from the under surface of the "body" to the posterior inferior angle of the base of the claw, for retraction and depression of the hooklet; and (2) a fan-shaped muscle, spreading out into the lower lips, and inserted into the anterior inferior angle of the base of the claw, for its elevation and protrusion.

Respiratory apparatus.—On the dorso-lateral surface, in the second segment, are two structures like minute gauntlets, with five stumpy fingers placed parallel with the long axis of the body, and opening externally by five small pores or ducts. These ducts are the external openings of two muscular tubes, which extend with numerous ramifications throughout the body; the branches given off divide and subdivide, and anastomose directly with those given off from the tube on the opposite side. Towards the hinder end of the larvæ these branches are again collected into two tubes, each of which ends in a disc-shaped depression at the extreme end of the dorsal surface of the tail; these discs have raised edges, and within each are seen three oval slits, which form the terminal openings of the respiratory tract.

The larva moves by striking the hooklets into the subjacent

surface and dragging the body after. When feeding, the hinder end of the body is shortened, and fixed by means of the sharp-pointed scales already described; the head and mouth are alternately raised and extended with the hooklets protruding, and then depressed with retraction of the hooklets, and by a rapid scratching movement the food is dragged into the mouth.

The larvæ were not true parasites (such as the Batrachomyia of McLeay), for they speedily destroyed the life of their host. Yet it was difficult to explain why the mouth and nostrils of batrachians were always the sole parts attacked. It was obviously impossible for the fly to lay its eggs directly in the toad's nostrils, and the probable explanation was that the eggs were laid in the toad's mouth whilst a pregnant fly was being swallowed. Evidence was given to show that the number of toads in certain years was largely reduced by means of the blow-fly's larva. For instance, in 1872 toads were remarkably plentiful in Tenby, South Wales, and the complaint was very prevalent amongst them; whilst in the following year scarcely any toads were to be found, and none were diseased. A similar sequence of events took place in the Isle of Wight in the years 1886–7. Parallel instances in which human beings had been attacked by the larvæ of these and other flies were given. Amongst others, Messrs. Coquerel and St. Pair, of Cayenne, had recorded many cases of convicts whose nostrils and eyes had been almost entirely devoured by the larvæ of the golden fly (*Lucilia hominivorax*) with fatal results. There is a specimen in the museum of the College of Surgeons which had been taken from the leg of Dr. Livingstone. Cases in which human beings had been affected were not at all rare, the larva of nearly every known fly having been found. *January 19th*, 1892.

XII. DISCUSSION ON PHAGOCYTOSIS AND IMMUNITY.

On February 16th, and March 1st and 15th.

THE PRESIDENT introduced the subject in a few words, in which he stated that the object of the discussion was to show how the blood dealt with morbid material introduced into it. He then called upon

Dr. WOODHEAD, who opened the discussion as follows:—Anyone approaching the questions that must be asked, and satisfactorily answered, before we can arrive at a definite conclusion as to the part that phagocytosis plays in the production of immunity against specific infective diseases, cannot but be struck by the difficulties with which each one is surrounded. Here, as in all great controversies, the personality, energy, and ingenuity of the supporters of opposing theories have much to do with the temporary success of one or another system, though not with the final issue. It is easy to prove anything to the credulous; it is an entirely different matter, and certainly a much more satisfactory one, in the case of those who are neutral, or who are absolutely incredulous. There is, however, no more satisfactory man to deal with than a friendly unbeliever; his objections stimulate our invention, and his candid criticism tests to the full not only our logical capacity but the soundness of our thesis. It is in a spirit of friendly unbelief, I hope, that we shall attack the arguments of those with whom we cannot agree; that we shall point out errors of experiment and faulty deductions, both direct and indirect, and that at the end of the discussion each one of us may carry away some additional facts, some new ideas, and the conviction that, if some of our experiments are without flaw,

others, interpreted in the light shed on them by the results obtained by other workers, may with advantage be repeated under various modified conditions, and with the exclusion of any factors by which some of them at least may be rendered fallacious.

It is impossible to discuss the relation of phagocytosis to immunity without introducing much concerning chemotaxis, and what has very aptly been spoken of as the humoral theory of immunity: the former of these is not necessarily antagonistic to—in fact, it may be actually looked upon as an essential part of—phagocytosis. The latter, however, is held as being in direct opposition to Metschnikoff's theory, though an attempt is now being made to combine them—an attempt which, though up to the present unsuccessful, or perhaps one should say founded on little experimental basis, is gaining ground with those who, with the observations and deductions of the earlier investigators at their disposal, have gone further into the matter. It would obviously be of no advantage that I should now attempt to make any suggestion even, as to which theory—the "phagocyte" or the "humoral"—is supported by the bulk of evidence; but it will be gathered from the short summary here given of the work that has already been done, that I lean to the theory of phagocytosis.

Taking first the question of phagocytosis from its physiological standpoint, and quite apart from its bearing on immunity, it has long been recognised that inert particles finding their way into the animal system, or even introduced into the blood immediately after it has been drawn from the body of an animal—the newt, say—are rapidly taken up by leucocytes. When this takes place in the body, the particles are in turn taken from the leucocytes by the connective, or other fixed, tissue cells. This, or a similar process, has been, and may be, observed by every pathologist who has examined a healing wound, a section of the lung, or the cells of a normal spleen. The significance of this process was first pointed out by Haeckel, who, comparing the leucocyte of the newt with those of the lower amœboid organisms, indicated that this must be the remaining evidence of a normal process of nutrition common to amœboid cells in whatever position they may exist; these cells, in taking into their substance vermilion or carbon particles, merely affording a better demonstration of what is always going on in most amœboid cells.

Then came the observation that the vacuoles in leucocytes appear

to be associated with the digestive and metabolic processes, partly as reservoirs for the accumulation of a digestive fluid, but more frequently for the accumulation of effete products.

In 1881 attention was first drawn to the part played by phagocytic cells in the production of immunity by Carl Roser, who, in an exceedingly interesting article, gave examples of the possession of this phagocytic power by the cells of both plants and animals, and of its importance in the resistance offered by them to the attack of the pathogenic fungi by which they are sometimes invaded. He maintained that the mobile amœboid cells of the animal body have the power of devouring, digesting, and assimilating, even those living active micro-organisms which in non-resistent or non-immune animals have the power of withstanding the attacks of the devouring cells, and of continuing their existence and carrying on their specific functions in the tissues and fluids, where, as he found, they give rise to their characteristic products and set up the special manifestations of the disease with which they are associated. He was convinced, indeed, by his own observations, that this power of taking up micro-organisms must be an essential factor in the immunity enjoyed by non-susceptible animals. It was at this point that Metschnikoff—to whose patient researches, fertile and ingenious experiment, and brilliant powers of deduction, we owe much of our knowledge of phagocytosis—took up the question, and, approaching it entirely from the experimental and biological sides, was able to build up, first a theory of phagocytosis, and then a theory of phagocytic immunity.

He confirmed Haeckel's observations, and further demonstrated the fact that certain amœbæ and flagellated or ciliated unicellular organisms depend upon bacteria and fungi, even under normal conditions, for much of their nourishment; these they destroy in large numbers, taking them into their substance, extracting from them all nutritive material, and then throwing out such matter as they cannot utilise. One of these small monads was observed to ingest within a few minutes, filaments of leptothrix ten times its own length. This observation is one of prime importance, but one which we are apt to lose sight of in view of the apparently more interesting questions that have arisen in connection with the destruction of pathogenic organisms. Here we have unicellular animal organisms composed of imperfectly differentiated protoplasm, utilising as nutritive material vegetable

unicellular organisms, first taking them bodily into their substance, and then rejecting what they do not require.

It can scarcely be maintained for a moment that these leptothrix filaments are deprived of their vitality before they are ingested by the amœbæ, and we must therefore accept it as a fact that these masses of elementary animal protoplasm can, under ordinary circumstances, deal with living vegetable protoplasm as a nutritive material, the process of digestion going on within cells which do not act merely in self-defence in taking up these lower bacteria or fungi, but are actually dependent upon this process of ingestion for their nutrition.

It is not necessary here to multiply examples of this process, as Metschnikoff's elaborate researches on this point, quite apart from the many who have followed in his footsteps, place the matter beyond all doubt. Here, then, is the first fact—that animal amœboid cells, brought into contact with certain of the lower vegetable organisms, retain their activity and their functions, whilst the vegetable cells which they have the power of ingesting are rapidly and completely destroyed. Going a step further, Metschnikoff demonstrated that in sponges the cells of one of the layers of specially differentiated cellular tissue—the mesoderm—of which the animal is in great part composed, may still retain this power of ingesting foreign particles, each cell in this layer playing the part of a single amœboid protozoon, and depending for its nutrition upon this intra-cellular digestion.

Phagocytosis in these cases, then, is not, as Cartwright Wood and I have elsewhere stated, an isolated factor or a function brought into play for a solitary or rare occasion, but a habit upon which the animal cell depends for its very existence. This fact comes to be of special importance when it is borne in mind that any "fundamental" function of undifferentiated protoplasm is always comparatively easily stimulated into activity, especially when its presence is again required. It is a fact which lies at the very foundation of the phagocytic theory.

Some time ago, whilst watching, along with Brook of Edinburgh, the development of the ova of the cod, the process of intra-cellular digestion was pointed out to me as occurring at certain stages in the whole of the cells of which the embryo is composed, small particles of yolk substance being taken into the actively proliferating cells, and clear vesicles, which we can only look upon as playing

a part in the function of excretion, making their appearance. Later, however, where the cells become differentiated, this intra-cellular digestion is confined almost entirely to the mesoderm-cells, and in the parablast layer the process of intra-cellular digestion is exceedingly well marked, the granules of yolk and the vacuoles standing out very prominently.

It may now be accepted as proved that in the metamorphosis of the tadpole, and of certain larval forms of insects, into fully developed forms, phagocytosis plays a most important part; but here it must be remembered that we are dealing with dead or partially devitalised tissues—tissues which have played their part and are now to be looked upon as effete matter, and therefore not to be classed under the same heading as living active bacteria. Degenerating muscles, nerves, and fascia are devoured by active amœboid cells, and in this way the rapid removal of effete material is effected, an enormous number of phagocytes gathering together to carry on the work at those points at which organs or parts have to be got rid of.

By a very natural extension, the part that this process of phagocytosis plays in the removal of dead or effete tissue after injury or disease in the higher organisms has also been traced; the destruction of the myelin sheath of nerve-fibres by amœboid cells, the absorption of bone by the large multinucleated cells that lie in Howship's foveolæ or lacunæ, the similar cells observed in myeloid sarcoma, especially in various tumours of the jaw where absorption of the bone is going on rapidly, the ingestion of fragments of yellow elastic fibre and the absorption of muscle, not only in the tadpole's tail, as observed by Metschnikoff and others, but also in the inflammatory process set up by the *Trichina spiralis*, as worked out so beautifully by Soudakewitch, and in the involuting uterus by Helme and others, have all been followed out. Bevan Lewis has also shown that the connective-tissue cells in the brain appear to exert a similar function in the removal of effete nerve-structures, a most important observation when considered along with the part that "association fibres" play in intellectual processes.

Although in the first instance much stress was laid upon the leucocyte as a phagocyte, Metschnikoff, even in his earlier papers, and later Wyssokowicz, evidently had in view the fact that many of the phagocytes were not true leucocytes, but that they were derived in some way or other from the fixed tissue-cells, which appear to undergo marked change under stimulation; they proliferate

rapidly, they lose their specialised forms, their branching processes disappear, and the nucleus comes to occupy a relatively large portion of the body of the cell. This nucleus as a rule remains single, but in all other respects the appearance of these cells approaches very nearly to that of the ordinary leucocyte, especially as such cells assume the specialised amœboid activity said to be so characteristic of the smaller cells. The single-nucleated macrophages, as distinguished from the small multinucleated microphages or leucocytes, must indeed be looked upon as the final phagocytes, though, as we shall afterwards see, they appear to have less marked powers of taking up living protoplasm than the leucocytes themselves, which in all essential respects approach much more nearly the primitive amœboid cells of the mesoderm-cells of the sponge, than do the large macrophages. The nearer the macrophage, under stimulation, approaches the microphage, the more aggressive does it become, and the less is it content to take up mere effete matter.

Even under normal conditions, then, these mesoderm-cells according to Metschnikoff, have as one of their functions the ingestion of all those solid parts of the organism that have become effete or useless; and where they are unable to carry out this function as individuals it would seem that they may combine in order to attack with greater certainty of success. As examples of this in the invertebrate kingdom Metschnikoff points out that the mesoderm-cell in the sponge may form a kind of network around bundles of leptothrix, gradually bringing about their destruction. In the same way it has been demonstrated by Geddes that particles of organic or other matter, when introduced into the abdominal cavities of certain of the echinoderms, may, if small, be taken up by single cells; but where larger masses have to be dealt with a considerable number of such cells appear to run together, the protoplasm becoming fused into a large plasmodial mass in which the individual nuclei of the original cells can scarcely be seen. Elsewhere I have indicated the part that myeloid or giant cells play in the absorption of bone and muscle, and also in the parablast of the ova of certain fishes. In this latter case, however, the multinucleated cells, in place of being formed by the fusion of single-nucleated cells, are the result of partial segmentation, the nuclei dividing but the protoplasm remaining intact as a single mass.

All this, however, has not led us beyond the point that amœboid cells in the higher animal organisms have the power, or rather the

function, of removing innocuous material—organic or inorganic—or at any rate material that has, in the quantities in which it is usually present in the organism, no deleterious effects on the phagocyte cells. This is a much more restricted function than that which is exerted by the single-celled amœbæ or by the mesoderm-cells of the lower invertebrate, which actually attack living organisms, and depend upon this power to a very large extent for their nutriment. It may be readily understood how in the process of development, where this attacking power is to a certain extent lost, being no longer necessary for the nutrition of the organism, the scavenging power may still remain, in order to get rid in the most economical fashion possible of dead or inert foreign particles, of chemical products, and of effete material of various kinds. Although this attacking power has in great measure been lost through disuse, it must be remembered that it still remains as one of the potential faculties of the primitive protoplasm, and that under suitable conditions it may again be brought into play; indeed, as Metschnikoff holds (and this is the key to his whole position), under certain conditions of stimulation the scavenging phagocytes may regain their original attacking function to such an extent that they may not only remove dead tissue and innocuous micro-organisms, but they may actually attack, ingest, and destroy micro-organisms to which, under ordinary circumstances, they would exhibit the greatest aversion, or to which, if they were brought into contact with them, they would inevitably succumb. We have here, as will be pointed out later, a special stimulation, and a stimulation that must be commenced gently, increased gradually, and carried on for some time; in fact, we may say there must be a gradual preparation or acclimatisation of the leucocytes in order that they may be able to contend at all successfully with pathogenic micro-organisms, and before it is possible for them to regain their phagocytic function from the nutritive point of view, a function that may become so marked that the secondary or scavenging function is relegated to a comparatively unimportant position.

Tissue resistance, which may be translated as the power of reaction of cells, is necessarily intimately bound up with the life-history of these cells, with their powers of nutrition, with the facilities that they have for the excretion of effete matter, their power of taking up foreign bodies (such as pigment, bacteria, and

the rest), and with their capacity for converting these into inert matter, and afterwards for utilising them for their own purposes, and of getting rid of the substances that remain. It must be remembered in this connection, however, that even the physical surroundings of cells, or the reaction of chemicals on the protoplasm of the cells, may interfere very greatly with some of these functions; and W. Pfeffer, in his careful observations on the action of aniline colours on vegetable cells, has pointed out what a great part the osmotic condition plays in inducing the absorption and retention not only of colouring matter held in solution, but also of solid particles brought in contact with the cells. He found, for instance, that on placing the cells of root hairs (and other vegetable cells easily examined) in a 3 per cent. solution of saltpetre or of citric or malic acid, methylene blue, which under ordinary circumstances is taken up with great avidity by the protoplasm of these cells, is utterly rejected. The same appears to hold good in the case of solid particles. So far as one can make out from a careful study of the results obtained by different experimenters, some such conditions as these may also play a part in determining the ingestion or rejection of living bacteria by the phagocytes.

It is not here necessary to give any description of Metschnikoff's original experiment made on the water-flea—the daphnia—with the *Monospora bicuspidata*—a form of single-celled yeast plant; but I would advise all who have not read his interesting paper to make themselves thoroughly acquainted with his most fascinating account of the behaviour of the needle-like spores of this parasitic yeast in the body-cavity, or in the tissues surrounding the intestine of its host. He shows how, when the small spore succumbs, it is taken up by the colourless blood-corpuscles or by the connective-tissue cells, and how it is developed into a rod-shaped vegetative form where these phagocytes, owing to weakness or inferior numbers, are unable to deal with it. Upon this observation the phagocytic theory of immunity was undoubtedly based, and following up this single observation Metschnikoff conducted a series of the most ingenious and well thought-out experiments that have been made since Pasteur's classical experiments on fermentation, and his work on the production of certain specific diseases.

I have pointed out elsewhere that erysipelas has been taken by the opponents of the theory of phagocytosis as an example which

supports their contention that phagocytes play only a secondary part, and that entirely a scavenging part, during the course of the disease. They point out truly enough that the streptococci in erysipelas are outside the zone in which the leucocytes are collecting, and that there is little or no evidence of inflammatory reaction for some time after micro-organisms have made their appearance in the lymph-spaces; and they argue from this that if the cells in the inflammatory zone play any part at all, it is only that of ingesting the micro-organisms that have been destroyed by the fluid elements of the lymph or blood. But it may here be observed—to use a homely phrase—that what is "sauce for the goose ought to be sauce for the gander," and that we have no more evidence of destruction by the fluid elements in the spreading erysipelatous zone than we have of their destruction by the leucocytes; whilst we have evidence that as soon as the tissues are stimulated to react in the zone outside the proliferating micrococci, the conditions under which the cells can carry on their phagocytic functions become infinitely more favorable, with the result that the disease becomes distinctly localised. Of this, however, I shall leave others who have worked specially at the subject to speak for themselves.

Let us see on what Metschnikoff depends for the proof of his theory of phagocytosis. At the outset we may indicate that he draws a marked distinction between leucocytes and those cells derived from connective tissue—a distinction, however, which does not seem to hold good in all cases, as it is evident from what we know of the life-history of cells, that extremely rapid proliferation of the connective-tissue or fixed cells, may take place under stimulation, and that under these conditions it is often extremely difficult, and one might say in some cases almost impossible, to distinguish between the cells derived from the two sources. Metschnikoff, indeed, indicated very early that many of the processes connected with the removal of the tadpole's tail were carried on by the larger fixed cells—a fact that was afterwards accentuated by Wyssokowicz, and again by Helme in connection with the absorption of muscular fibre, by Metschnikoff himself, and by Soudakewitch. However, for our present purpose we may take the leucocytes as representing the phagocyte-cells, and anthrax—a disease on which much of the really accurate work on acquired immunity has been done—as the typical disease. In immune or resistent animals anthrax bacilli, which may be deeply stained with

vesuvin or methyl blue, are invariably found within these cells, not only at the point of inoculation, but also in the blood. It has been objected that this colouring of the bacilli by aniline colours affords no proof that the organisms were not killed before they were taken into the substance of the cell—a perfectly legitimate criticism, as we know that bacteria killed by heat, by bichloride of mercury, or by absolute alcohol readily take up the various staining reagents. It has, indeed, been proved by Mitchell Prudden and Hodenpyl that tubercle bacilli killed by being boiled for two hours and then injected into the circulation of an animal, will still take up aniline stains, and that these dead bacilli may often be seen as brilliantly stained rods lying in the tissue spaces, and in some cases actually within the cells, even six weeks after they have been injected.

This at first sight would appear an almost insuperable difficulty, but Metschnikoff by the following experiment demonstrated that bacilli imprisoned within the leucocytes taken from immune animals still retain their power of vegetative reproduction. He placed some leucocytes containing these bacilli on a warm stage under the microscope, and by most delicate manipulative measures he isolated three cells, each of which contained anthrax bacilli; each cell was taken up in a sterilised capillary tube, from which it was transferred to nutrient bouillon, and was carefully and continuously observed under the microscope; after a time the bacteria were seen to develop in length, and when they were transferred to larger quantities of a sterile nutrient medium a pure culture of the anthrax bacillus was obtained. Further, he has been able to demonstrate that although in immune animals the process of digestion goes on first in the leucocytes or microphages, not only microphages with their contents, but also free bacilli are afterwards taken up by macrophages, most of which appear to be derived from local fixed cells, though some may possibly come from a distance.

Another proof that these micro-organisms retain their vitality is that although in most cells bacteria are undergoing degenerative changes, and do not take on staining material at all readily—their protoplasm becoming granular, or a great part of it being absorbed, whilst the nuclei of the devouring cells still remain distinct and deeply stained, vacuoles associated with rapid metabolic changes also being present—in some cases the cells are being actually broken

down, although many of the bacteria within them are as perfectly stained as are those taken from a pure fresh culture. This appears to be the case especially where a large number of bacteria are contained within each cell, and where it would appear that the protoplasm of the cell has become exhausted through over-stimulation, and where in consequence the bacteria have gained the upper hand.

Frank, objecting to this observation, and as the result of his own experiments on white rats—in which he was able to obtain the death of one only out of twenty-two, although all the others had local anthrax lesions,—maintains that the bacilli are killed *in situ* by the bacteria-killing serum which passes through the spaces in which the bacteria are confined. He says, however, that although the bacilli were localised first by the density of the tissues into which they were introduced, and second by the accumulation of leucocytes around them, they could never be demonstrated in the leucocytes. Metschnikoff, on the other hand, working under similar conditions, found that in the cells that accumulated in this part it was a comparatively easy matter by means of the use of special staining reagents, such as methylene blue, to determine the presence of bacteria; he therefore holds that such cells are true phagocytes, and he further argues that Frank's experiments, in place of being contradictory, bear out his theory in a most remarkable manner.

It has for long been known that certain lower organisms exhibit a decided liking for some substances, whilst for others they have an instinctive aversion; and as the result of numerous observations it would appear that they are specially attracted to materials which may be utilised in the process of nutrition (trophotaxis). Such organisms exhibit a marked indifference to substances from which there is nothing either to be gained or to be feared; whilst for other substances, most of which seem to exert some paralysing or other deleterious effect on the cell, they evince the greatest dislike. Gabritchevsky,[1] in summarising this chemotactic action of leucocytes, gives a very good account of what has already been done. De Bary observed that in myxomycetes there were certain solid substances which, when brought near the plasmodium, exerted a vigorous repellent effect, the plasmodium in the first instance getting out of its way as rapidly as possible. If, however, these substances, with definite chemical characters, were introduced

[1] See also Adami, J. G., 'Medical Chronicle.'

sufficiently gradually, the organisms would, after a time, become habituated to their presence, and would then actually take them up into their protoplasm. Metschnikoff, starting from his own observations, had already conceived the idea that the acquired immunity against certain diseases might be due to a similar process of acclimatisation of the cells, as a result of which they are enabled to carry on their phagocytic functions in the presence of what, under ordinary conditions, would not allow them to come into sufficiently close contact to permit of their ingesting the microbes. This process of acclimatisation can undoubtedly be brought about if the conditions be modified gradually and slowly; and it is now well known that cells, which at first would be quite incapable of reacting in the presence of a specific poison, may ultimately be able to survive in the presence of large doses, and even exert their special phagocytic function.

It is now a well-recognised fact that if doses of poisons, produced by a specific bacillus, paralyse amœboid cells, these same cells may by careful preparation, by the administration of repeated—at first small but gradually increasing—doses of the same poison, be so habituated to its presence that, after a time, the paralysing effect is no longer excited, and the phagocytes are able to treat pathogenic organisms as comparatively inert foreign bodies, and the disease of which these organisms are the ultimate etiological factor is kept under control as the phagocytic cells destroy the organisms. The organisms may indeed remain in the body for some time, they may reproduce their poison, but the prepared cells are now able to carry on the scavenging functions even under the disadvantageous conditions to which they are exposed, and in time the whole of the micro-organisms are taken into the cells, and, being unable to carry on their reproductive processes at any great rate, are gradually destroyed.

In marked opposition to Metschnikoff's theory, it was early claimed by Emmerich and Mattei that the property of destroying bacteria was vested in the fluid constituents of the blood. They first maintained that these *antibiotic* fluid constituents were the result of the activity of the bacteria themselves; in fact, they took up the retention theory. After further observation, however, they receded from this position, and came to the conclusion that the *antibiotic* substances were formed by the living cellular elements. Following them, Flügge, Nuttall, and Nissen, who were

afterwards joined by Buchner and others, described a bacteria-killing substance which was present in the blood of immune animals not only while it was circulating in the vessels, but also after it was withdrawn and had practically undergone coagulation, the serum being separated from the corpuscles, in which condition the blood might be said to have lost every trace of vitality. They hold, therefore, that a certain quantity of a toxic material is present in both living and dead blood, which apparently has little or nothing to do with the blood as a living tissue or fluid of the body (in this differing from von Fódór's original idea, which was that there existed in the blood-plasma a vital element which killed off the micro-organism). Following this up, Buchner maintains that the cause of recovery from an attack of an infective disease is directly due to a bacteria-killing action of the serum, and he further holds that phagocytosis is brought about merely by the dead microbes giving up their proteins, which, acting chemically in a positive manner, draw the leucocytes to the point at which the organisms are breaking down; here the leucocytes take them up, and ultimately digest and get rid of them, so that he looks upon phagocytosis merely as the result, first, of chemotaxis; and secondly, of an effort on the part of the organism to get rid of the devitalised microbes. He admits that phagocytosis occurs only in those cases in which an effort is made on the part of the organism towards recovery, and that it is present only where an animal enjoys a certain measure of protection.

Buchner claims, then, that phagocytosis is entirely the result of positive chemotaxis, which in turn, so far as micro-organisms are concerned, can only be influenced by their proteins, and that specific toxines can have little or no influence on the process. In support of this thesis he points out that Roux and Metschnikoff, both of whom believe thoroughly in the importance of the *rôle* played by phagocytosis in the production of immunity, appear to hold different views as to the chemotactic action of these toxines on leucocytes—Roux indicating that they have a positive action; Metschnikoff, on the other hand, leaning to the opinion that they are negatively chemotactic, and that they repel the leucocytes. This, however, does not appear to be an insuperable difficulty, for we have ample evidence that the same substances in different strengths of solution and under different conditions may exert very different chemotactic actions; and that where one strength of solution may actually repel

leucocytes, a more dilute solution may cause attraction. In this connection we shall probably have the pleasure of seeing some of Dr. Ruffer's specimens, in which may be well seen the effect of antiseptics, in different strengths, on leucocytes. I need not repeat to this Society Lister's classical experiments on the effect of heat on the movement of the cilia of a cell, but I may be allowed to notice that Schultze was able to show that the ferment power of yeast is distinctly increased by the addition of extremely dilute solutions of corrosive sublimate, arsenic, carbolic acid, and iodine, all of which in stronger solutions exert a very deleterious effect upon the protoplasm of the cells; every irritant exerting an action on every living cell, the cell activity varying greatly according to the intensity of the irritation set up, increasing for a time when it is more intense, but rapidly diminishing after a certain point has been reached.

In order to overcome the objection of those who maintained that the organisms are killed by the fluids of the blood, and not by the cells, he took small boxes made of rose pith or of the pith of the common reed (*Phragmites communis*), placed within them the spores of pathogenic organisms, and then introduced these into the veins of certain animals, into the lymph-sacs of the frog, or into little pockets under the skin of immune animals. The pith, for a time acting as a filter, kept out the cellular elements, and kept in the anthrax bacilli, but allowed of free circulation of fluid through its interstices. He found that not only were the organisms not injured by the fluid, but they were actually enabled to vegetate and increase—in some cases very rapidly—in number.

Ruffer, who will probably give you the result of his own experiments, confirmed these observations, and pointed out, moreover, that the passage of generations of certain pathogenic organisms through the fluids of the body actually rendered them considerably more virulent—a result for which we had been prepared by Metschnikoff's experiments on the increase of virulence of anthrax bacillus passed through pigeons.

Roux and Metschnikoff maintain, further, that leucocytes may become accustomed to the presence of considerable quantities of toxines in those cases where there is acquired immunity, and this appears to be undoubtedly the case in many diseases. In favour of the humoral theory the single doubtful case of the *Vibrio Metschnikovi* can be brought forward, for here it has been shown that

even a guinea-pig, immune to the subcutaneous injection of the organism, still remains remarkably susceptible to the action of the toxines, though even here it is maintained that if the habituation be brought about very gradually, the protection extends also to the poisons. In this case it is supposed that we have stronger evidence of the correctness of the humoral theory than in the case of any other disease, as it is held by Behring and Nissen that the serum from susceptible guinea-pigs affords a favorable medium for the growth of this organism, whilst that of immune animals kills them in five hours. On the other hand, Metschnikoff has pointed out that the *Vibrio Metschnikovi* will grow in its normal form in the fluids of an immune animal, although when the same organism is cultivated in similar fluids removed from the body, involution forms are of frequent occurrence. Here, then, we have a marked difference between the behaviour of the organism in the living medium and that in the dead serum. It is evident that in this instance at least the fluids must have undergone some marked change during or on their removal from the body, especially when it is borne in mind that the micro-organism remains alive for at least a fortnight after it has been introduced into the anterior chamber of the eye of a protected guinea-pig. Roger made a similar observation on the streptococcus growing in the serum of immune rabbits, the organism growing freely, but rapidly becoming attenuated. Roger and Charrin noted the same in connection with the *Bacillus pyocyaneus.*

It must be borne in mind, however, that even Metschnikoff does not maintain that phagocytosis is the only factor in the production of immunity. He claims merely that in immune animals it undoubtedly plays an important part, as here, through the agency of the leucocytes and the proliferating connective-tissue cells, living pathogenic bacteria are removed from the circulation; they are prevented from germinating, and thus the number of organisms is gradually diminished. He holds, moreover, that it is by this process of phagocytosis that diseases are localised, and that from the very fact that we have a local reaction in immune animals we have an indication that the phagocytes are reacting to prevent the spread of the organism beyond the point of its introduction, and that thus we have, as it were, a first line of defence which must be passed before the disease can become generalised; and that in the endothelial cells of the spleen, of the blood-vessels, and especially

of the minute vessels of organs in which there is free capillary anastomosis and slow circulation, we have what may be called a second line of defence, and that when this is broken down the animal must necessarily succumb to a generalised disease.

In an article on the recent researches on immunity, Adami suggests that there may be an increase in the bacteria-killing power of the blood-plasma through the dissolution of a number of the white corpuscles. It is well known that the breaking down of such corpuscles sets free materials which induce positive chemotaxis, and stimulates into greater phagocytic activity those cells which remain intact. In this case there appears to be some doubt as to the increased bactericidal power as the result of the setting free of the elements of the leucocytes. Working at this from one point of view, Wright has been able to demonstrate that anthrax bacilli may actually be cultivated on the broken-down leucocytes; further, it has frequently been demonstrated that quinine in large doses exerts a very marked action in destroying leucocytes in the animal body, and for that reason it was anticipated that to this action quinine owed the beneficial results obtained from its use in certain specific fevers.

Wood and I, using this drug in cases of anthrax, found that in every case the animals treated with quinine died more rapidly than the controls—a most remarkable fact, and one which, taken in conjunction with Wright's observations, appears to negative Christmas's, Hankin's, and Adami's suggestion as to the setting free of bactericidal material from dead leucocytes. Were it proved, however, we might, from our experiments make the very important deduction that the cells in a living condition exert a greater protective influence than they do when dead and disintegrated, as even the control animal, in which the quinine has not been present to help to break down the leucocytes, lives longer than that in which the bactericidal power of the fluid is supposed to be increased by the diffusion into it of the elements of the broken-down blood-corpuscles. This is the more remarkable when we find that almost all those who believe in the bactericidal power of dead blood-serum assign to it a much greater efficacy after it is withdrawn from the body than when the living plasma is left circulating in the vessels. They assume that it has a much greater bactericidal power; if that be the case this power must, to a certain extent, be inhibited within the body. Even here, however, we are confronted with another

difficulty, as a large proportion of leucocytes remain active after they are removed from the body.

Lubarsch believes with Flügge that the bacteria-destroying power of serum is exhausted by use, and that if the number of micro-organisms introduced is larger than that with which they can deal, the animal must succumb. Metschnikoff, however, has been able, in certain partially protected animals, to demonstrate the presence of living bacteria four days after their first introduction into the tissues. This would indicate—if the power of killing organisms rested solely or mainly in the fluid elements of the blood—that, in cases which recover, these organisms had, as it were, been waiting their turn to be killed off, the supply of poison not being equal to the demand; or, on the other hand, we must assume that here we have a condition of almost perfect physiological equilibrium, those organisms that are not destroyed being just able to produce a few more than the next batch of poison can deal with, so that unless some other element comes in, such as increased production of poison, or the calling in of the phagocytes to help in the work of destruction, the multiplication of bacteria might go on indefinitely.

One of the great sources of error in connection with this question is the assumption that immunity against different diseases must always be obtained or acquired in the same way. It is evident that the processes by which immunity can be obtained must vary as widely as do the processes of disease themselves. As Lubarsch points out, tetanus and diphtheria and their manifestations are totally different from anthrax and the processes associated with its presence. The primary mechanism of the diseases are absolutely unlike, while the same may be said as regards typhoid and tuberculosis. Tetanus and diphtheria must be looked upon as toxæmias or septicæmias, using this term in the sense in which it was used some few years ago. The organisms which produce the poison are strictly localised to a very definite area around the point of introduction, but they form poisonous substances which, taken into the circulation, give rise to marked disturbances and degenerations, especially of the highly organised tissues, such as the nerves, muscles, and excreting epithelium. One can understand what an injurious effect such poisonous material must have on the tissue-cells, and even on the leucocytes, at the point where the poison is introduced, especially if these poisons are introduced at once in a virulent form; the cells are paralysed, they are at

once attacked by the organisms, and form a nutrient substratum on which these organisms can grow. If, however, the cells can be habituated to the presence of small doses of poison it is quite conceivable that eventually we might produce an immunity, from the fact that we had acclimatised the animal to larger doses of the poison than the micro-organisms when introduced could secrete; the cells would then be able to carry on their destructive functions, and thus get rid of the organisms before they could do any harm. As a matter of fact, it has been shown that the tetanus organism, unless accompanied by a considerable quantity of its specific poison, is absolutely unable to flourish in the healthy tissues, so that in this case, at any rate, the immunity has to be acquired against the action of a poison formed by the bacillus, and diffused into the body, rather than against the growth of the bacillus itself.

The same holds good to a certain extent in the case of diphtheria, the conditions necessary for infection by this organism appearing to be either (1) inflammations of the mucous membrane, accumulation of secretions, formation of ulcers, and similar conditions, or (2) the introduction of a considerable mass of the organism, accompanied by a quantity of the specific poison. In both cases it is probable that in conferring on the animal a certain degree of protection we may actually set up temporarily a series of degenerative changes so characteristic of diphtheria.

It is probable that similar changes may be found in animals that have been protected against tetanus. In the case of anthrax it is necessary to produce an immunity (1) which will localise the disease at the point of introduction, or (2) which will enable the tissues to act on the organism at once—probably in the first case through the leucocytes, for we can scarcely imagine that a sufficient quantity of the fluid elements of the blood can be brought up to attack a large number of organisms, when the blood of the whole body, according to Lubarsch, can determine the destruction of the comparatively small number of 10,000 anthrax bacilli. Even a very high degree of alteration in the bactericidal power of this fluid would scarcely enable it to deal with the large numbers that are often, in experimental work, introduced locally. Only some such factor as the bringing up of large numbers of leucocytes, which, owing to a natural or acquired immunity, are enabled to act in the presence of anthrax poison, can bring about, first, a localisation of

the anthrax bacilli by the erection of a cellular barrier, and second, their destruction by a process of ingestion and digestion.

In all our researches on immunity we are confronted with the question, How is it that immunity is conferred for one disease only, or certainly for one series only? Why should an attack of vaccinia or variola be necessary to ensure protection against another attack of variola? The exhaustion or assimilation theory was very early found insufficient to account for this, as it was also to explain the different action of the *Bacillus prodigiosus*, which, whilst diminishing the action of a dose of *Bacillus anthracis*, increases the virulence of Chauveau's bacillus—the bacillus of charbon symptomatique. Similarly, the local immunity theory was found insufficient, and local inflammation as a factor in immunity has also had its day and has passed from the scene, perhaps, however, to be revived at no distant date. The adaptation theory, or cellular chemical theory, advocated by Klebs and Grawitz, Ribbert's theory of massing of leucocytes, and Metschnikoff's phagocyte theory, have in turn ousted the retention theory advocated by Wernich and Chauveau, whilst the serum bactericidal theory has come forward to rout this if possible. It may be that we may have to cull something from each of several of these various hypotheses, but we must always bear in mind that the potential forms and functions of animal protoplasm are as great as the number of directions in which it actually develops. Its property of resistance to any special poison, or its power of carrying on its functions in the presence of such poison, can always be brought about by exercise. It falls into abeyance, no doubt when not required, but once revived it is far more readily brought into play when again called upon to exert its specific powers. Each poison, it is held, develops or recalls a special resistance, and it is in the rapid development of this special resistance that immunity consists.

Even should the bactericidal power of serum be proved to exist, it must depend directly upon changes produced in the living cells, changes which must be equally specific, if what we think we know about immunity is at all to be trusted. Immunity is specific, whilst this bactericidal power of serum is very general in its action, unless we accept it that the blood must be loaded with a fresh bacteria-killing material for every disease we contract from childhood upwards, beginning with whooping-cough and measles, and ascending the whole gamut of ills that flesh is heir to.

Professor BURDON SANDERSON.—As the subject which we have to discuss this evening is one on which we all hope to receive much valuable information from members of the Society who are actively engaged in researches relating to it, I will speak very shortly; and, with this view, I may as well begin by saying that I cannot accept the doctrine of Phagocytosis. I am opposed to it, first, because the facts as to the part taken by leucocytes in pathological processes do not seem to me to make it necessary to suppose that they possess such special attributes as the theory assigns to them; and secondly, because the theory itself seems to me inconsistent with certain principles which may be considered axiomatic in physiology and pathology.

In the conception of an organism the idea of development and self-maintenance is a fundamental one—the idea, I mean, that the organism maintains its form and function in accordance with a normal from which it does not readily depart. To us as pathologists this manifests itself most obviously in the power which the organism possesses of recovery from injury or disease—of returning to the normal the moment that the exciting cause ceases to operate. Nor would any of us hesitate to include in this general power of recovery the more specific power which now interests us —*the power which the organism possesses of protecting itself against specific infection.*

What we have now to inquire is not whether this power exists, but how it is exercised. We have to discuss in what susceptibility and insusceptibility, immunity and the want of it consist, with special relation to the question *whether it is dependent on the special endowments of leucocytes.*

The theory of Phagocytosis asserts nothing less than this, that the development of an infective process in the organism is prevented by the action of leucocytes at the seat of infection. What we have to determine is (1) whether the organism cannot be shown to exercise its self-protective power irrespectively of the intervention of leucocytes; and (2) whether their intervention is dependent on any *specific* relation between them and the *specific* properties of the infective agent.

The first question I must leave to another opportunity. I will limit myself to the more general one of the alleged specificity of leucocytic function.

What has been ascertained about it is, so far as I know, (1)

that in a considerable number of instances *morbific agents* in a tissue give rise to the swarming of leucocytes at the seat of infection; (2) that in general there is a remarkable coincidence between this phenomenon and the resistance which the organism appears to offer to the development of the infective process—in other words, to its susceptibility; and, consequently, that it may be inferred that the activity in question is beneficial. So much I believe and all pathologists admit; but what we say is, that all the observed phenomena relating to leucocytes can be accounted for as an expression of the recognised physiological properties of these cells. These properties, as ascertained by experimental investigation of the last thirty years, are, (1) amœboid motion; (2) the power of incorporating; (3) that of migration. It is on these properties that the whole question turns; for, as I have said, we hold that the part leucocytes play in the struggle between organism and morbific agent can be explained by reference to these ordinary endowments. The advocates of phagocytosis, on the other hand, say that these endowments are inadequate, and that we must assign to phagocytes a much higher and more specialised faculty, namely, a specific relation between them, and each of the various morbific agents to the invasion of which the organism as a whole is susceptible.

About amœboid motion and intussusception nothing need be said. We have been acquainted with both for thirty years, and for twenty years at least they have been familiar to every one, although of course it was not until Metschnikoff entered on his long and laborious studies, extending over so enormous a range of physiological and pathological examples, and brought to bear on them improved histological methods, that we knew these facts in detail.

As regards the third of the three properties to which I have referred, the fact that leucocytes so long as they are in a normal state are attracted by a variety of chemical substances, but especially by protoplasm in a state of approaching devitalisation or effeteness—in other words, by damaged tissue, is one with which we have become familiar only recently. We owe our knowledge of it to very recent work, especially to the researches of Buchner, of Massart and Bordet, of Gabritschewsky, and particularly to the recent inquiries of Dr. Rüffer.

I have elsewhere indicated the great importance of these pheno-

mena in relation to the doctrine of inflammation, in which what is now understood by the word "chimotaxis" has filled a long-recognised blank. This property of being attracted to any part where mischief is going on is not only an intelligible one, but serves to bring the process of suppuration into intelligible relation with such physiological facts as relate to the agency of leucocytes in the removal by absorption of effete parts (such, *e. g.*, as the tail of the tadpole). It also serves to explain why in the infective process it happens that leucocytes congregate to the focus of infection. They do so not because they are allured by the morbific poison itself, but rather because they have an appetite for the damaged tissue by which it is surrounded.

Accordingly we should expect the question whether or not the swarming of leucocytes should occur in a particular instance to depend on two things: (1) on the presence of local action, and (2) on the condition of the leucocytes themselves; and that the phenomena would fail to occur either when the local action is absent, or when it is excessive—in the first case from the absence of damaged protoplasm, in the second from the saturation of the leucocytes with the alluring material.

Morbid poisons of which the local action is intense produce no inflammation; those which are feeble, also none. The favorable condition is between the two.

Now, although this allurement is a very surprising phenomenon, there is nothing specific in it. It is a general property of leucocytes in which other similar cells participate. If we are right in thinking that this, taken with the other properties of leucocytes, enables us to understand their participation in specific infection, there is no reason whatever why we should endow them with powers scarcely short of intelligence.

The position, therefore, which we desire to take is not that the agency of leucocytes is unimportant—very much the contrary; but that the specific power which the organism possesses of resisting a specific infection (whether that power be original or acquired) belongs exclusively to the organism and to its parts; and consequently that leucocytes, being independent organisms, no longer participate in it.

That the activity of leucocytes, like everything else in the organism, works together for the general good cannot be questioned, but it is just as unreasonable to attribute to them a prophylactic

motive as it would be to suppose that the leucocytes which aid in the absorption of the effete tail of the tadpole are anxious to provide for the convenience of the future frog.

Dr. KLEIN.—I also wish to declare my colours at the outset and to acknowledge myself a free-lance, if by this is meant one who holds a strong opinion on one side. The points which I wish to bring forward in this discussion may be arranged under the following heads:

1. There seems to exist a misunderstanding on many sides as to the exact meaning of "phagocyte." A "phagocyte" is not simply a cell which includes in its interior living microbes; Metschnikoff himself was, in the earlier phases of discussing his theory, constantly bringing forward such arguments, and some of his pupils do so still even to the present day. This is manifestly not the case, because cells may contain in their interior living bacteria and yet have nothing to do with a destruction of the bacteria; on the contrary, such cells are being themselves destroyed by the bacteria —(*a*) gonorrhœa; (*b*) Egyptian ophthalmia, malignant œdema and pneumonia, swine erysipelas, mouse septicæmia, diphtheria; (*c*) tuberculosis; (*d*) leprosy; (*e*) malaria, relapsing fever, psorospermosis. In these diseases cells occur which contain living microbes, but you cannot speak of them as phagocytes because no destruction by them of bacteria takes place; on the contrary, the cells themselves are being destroyed by the bacteria, and you ought to speak of the bacteria as *cytophages*.

2. The cases which are quoted as offering examples of a real destruction of the bacteria by leucocytes are the cases of insusceptibility, in which the specific microbes do not multiply within the animal body, and are taken up and destroyed by the leucocytes; this "*mechanical theory of phagocytosis*" is said to constitute immunity. Now, is this true in all cases of immunity? No, there are certain well-established cases in which it certainly is not true. (*a*) When the bacillus of swine erysipelas is subcutaneously injected into a rabbit made previously refractory, the destruction of most of the bacilli is complete long before a leucocytosis is present. Metschnikoff's observations as to the occurrence of some living bacilli even forty-eight hours after do not negative this. (*b*) Anthrax inoculated in rats and in dogs; here it is extremely difficult to find a phagocyte at the seat of inoculation. (*c*) Anthrax bacilli

injected into the dorsal lymph-sac of the frog; Petruschki's, Fischel's, and my own experiments prove that destruction of bacteria occurs long before any phagocytosis. Long before leucocytes have taken up the bacilli are there already bacilli degenerating and destroyed. Besides, the battle is not limited to the lymph-sac at all. From this it follows that in these cases other agencies are at work which destroy bacteria.

3. Lymph and serum and plasma free of cells are powerful destroyers of bacteria; the experiments of Buchner, and especially Sanarelly and others, prove this conclusively.

4. The experiments of Ogata, Hankin, Behring, Tizzoni and Cattani prove that an animal may be made insusceptible by the injection of lymph and serum and other albuminous substances derived from immune animals. Is there one particle of evidence to show that this is brought about by changing the nature of leucocytes—that is to say, that the injection of these substances into an animal incapacitates the cells from acting as phagocytes? In the narcosis experiments on frogs and rats by myself and Coxwell there was nothing of such a change perceptible.

5. There exist, however, cases in which with immunity a simultaneous taking up of the inactive microbes by the leucocytes does take place. But does this prove that the phagocytosis is the primary, *i. e.* the essential factor? By no means. Nobody doubts that leucocytes are able to take up bacteria, just as they take up other granular matter; these facts have become familiar to everybody. That this means a taking up of them for the object of destruction, *i. e.* for the production of immunity, has not been proved, and there are observations to hand which indicate that something else first acts on the bacteria, and then the leucocytes are capable of taking up and removing the bacteria, *i. e.* acting as scavengers. All the cases brought forward by Metschnikoff and his adherents find a ready explanation in this theory; these observers err inasmuch as they take no account whatever of the biochemical changes that are going on, they leave out of account the whole of the evidence which shows that the tissue juices themselves are bacteria destroyers, and they forget that for the sake of proving immunity by the mechanical theory, you have to prove that in all these cases the destruction is not carried out by the tissue juices. The local leucocytosis which is observed after inoculation need have no more to do with phagocytosis than in

those instances in which leucocytosis is brought about by chemical means, by tuberculin, and in Prudden's experiments by sterilised tubercle bacilli. In some instances leucocytosis follows the inoculation of attenuated virus, *e. g.* in pneumonia, diphtheria, glanders in rabbit; in others no leucocytosis at all follows, at any rate not for some days, during which time the bacteria gradually die off, no phagocytosis being present. The most feasible theory is that advanced by Buchner, viz. the tissue juices weaken and destroy the bacteria, and in some cases, but by no means in all, the bacterial products or their substances (albumens) attract the leucocytes, and the bacteria themselves are taken up by the latter and removed; in other cases it does not come at all to such an attraction, and then no taking up of the bacteria by the cells occurs.[1]

Mr. Kanthack.—Taking phagocytosis in connection with immunity to mean the ingestion and digestion of living micro-organisms by certain wandering or fixed cells of the body, I assume that, at the present date, no doubt exists as to the occurrence of such a phenomenon. Phagocytosis is almost universally observed in cases where an animal recovers after being inoculated with a pathogenic germ, or where an animal, artificially or naturally immune, is inoculated in the same manner. It has been claimed that phagocytosis is the chief, if not the only factor concerned in the acquisition of immunity.

I would abstain from alluding to the origin and nature of the phagocytes, were it not that Dr. Ruffer—as far as I can follow him—asserts that all phagocytes, including microphages and

[1] Dr Klein's remarks were illustrated by the demonstration of a number of photographic lantern slides of cells containing bacteria.

1. Gonococcus.
2. Bacillus of Egyptian ophthalmia.
3, 4, 5. Bacillus of tubercle, human, from rabbit's lung, from rabbit's liver.
6. Bacillus of malignant œdema, aërobic.
7. Bacillus of swine erysipelas.
8. Bacillus of diphtheria.
9. Bacillus of grouse disease in the guinea-pig.
10. Bacillus of grouse disease in the mouse.
11. Bacillus of leprosy. 11 *a*. Leprosy.
12. Bacillus of influenza.
13. Anthrax in the immune frog.
14. Anthrax in the frog dead of anthrax.

macrophages, plasmic and epithelioid cells, are derived from leucocytes. On the contrary, there can be no doubt that the plasmic and epithelioid cells observed during inflammation and regeneration are derived from the fixed connective-tissue cells *in situ*. This has been shown by the researches of Grawitz, Ziegler, Nikiforoff, Bardenheuer, and also by Messrs. Ballance and Sherrington. Personally, I have on several occasions repeated the experiments of Grawitz and Bardenheuer, and cannot accept Dr. Ruffer's views.

The question at issue is "whether immunity from infective diseases or lesions is caused by phagocytosis, *i. e.* through the phagocytes alone and through nothing else." Though phagocytosis may be constantly observed in immune animals, it may for all that be simply a concomitant physiological effect or change due to the acquired immunity. I shall only discuss acquired immunity, for it is evident that the only logical method to study the process of acquiring immunity is by means of considering the changes in the organism while passing from a non-resistent to a resistent state. Personally I think that, at the present state of knowledge, we cannot accept any one theory as exclusive; but though acknowledging that phagocytosis is of great importance as a protective mechanism, I am unwilling to accept the exclusive phagocytic theory, believing that the acquisition of immunity rests on a much broader basis than the voraciousness of the leucocyte.

I shall discuss only three chief points, as it is impossible to allude to all the various matters in the short time allotted to me. These points are (1) the *influence of the body fluids*; (2) *chemotaxis*; (3) *phagocytosis*.

I. *Do the living fluids of the body play no part in the production of immunity?*—The serum of many animals has a marked bactericidal power outside the body, but we cannot establish any general law, because there is no necessary correlation between the natural insusceptibility of an animal to a disease and the bactericidal power of its serum over the microbe causing such disease. This has been put forward as a grave objection to the so-called humoral theory; but I think wrongly, for it is to my mind impossible to draw any logical inference as to the artificial causation of immunity by contrasting a naturally immune animal with a naturally susceptible one. In future experiments should be made in such a manner that the bactericidal power of the serum of a naturally susceptible

animal be tested (*a*) before it has been immunised, and (*b*) after it has been artificially immunised.

If then any law can be established, we must expect to find one or more of three conditions, viz. after the acquisition of immunity the serum should be (1) either more bactericidal, (2) or possess greater attenuating power, or (3) possess greater destructive power over the tissues of the microbes.

It is too narrow to judge by the bactericidal power alone, for it is impossible to disconnect the bacteria from their metabolic products, and it is these which cause the disease. As long as the poison is not neutralised, it matters little whether the bacilli are eventually killed or not.

To give examples, we find (1) under the first heading that the serum of a guinea-pig after artificial immunisation kills the *Vibrio Metschnicovi*, and that the serum of a guinea-pig after artificial immunisation has greater bactericidal power over the *Bacillus Chauvæi*.

As an exception we may mention the serum of a sheep protected against anthrax. But, on the other hand, Christmas succeeded in extracting from the organs of an immunised rabbit a substance which had greater destructive power over the anthrax bacillus than a substance similarly extracted from the organs of an unprotected rabbit.

According to Bouchard, it has been proved for nine infective processes that the serum of the immunised animal has greater bactericidal power than the serum of the same animal in the non-immunised condition. These are anthrax, charbon symptomatique, cholera, erysipelas, diphtheria, tetanus, pneumonia, and the lesions caused by *Vibrio Metschnicovi* and the *Bacillus pyocyaneus*.

(2) Under the second heading we find that the serum of an immunised rabbit attenuates the streptococcus of erysipelas, and the serum of an immunised rabbit attenuates the *Bacillus pyocyaneus*.

(3) Under the third heading we find that the serum of an immunised animal neutralises the tetanus toxine, the serum of an immunised animal neutralises the pneumotoxine, and the serum of an immunised animal neutralises the toxine of diphtheria.

Experiments in these directions and on these lines should be extended.

Now it is true that an experiment in a test-tube with ante-

mortem or dead serum we cannot immediately apply to the changes and action of the living fluids. But we must not be too dogmatic, and say, "because the serum of the naturally susceptible guinea-pig is more destructive to the *Bacillus Chauvæi* than the serum of the naturally less susceptible rabbit, *ergo* test-tube experiments prove nothing." Such an experiment is not crucial.

Some test-tube experiments are almost conclusive. I am alluding to the action on tetanus toxine of blood freshly removed from an immunised animal.

Anyhow, we may claim that test-tube experiments logically conducted are suggestive. For the serum is, in the first instance, derived from the plasma; and if we find constant changes in one or other direction after artificial immunisation, it is reasonable to suspect changes of similar nature in the plasma and body fluids also. With Bouchard we cannot possibly consider this almost constant increased bactericidal power over a particular microbe, after immunisation against such microbe, a mere test-tube accident!

I can only allude to some of the many objections offered. These should always be examined in the light of logical evidence, and if derived from experiments on animals of two absolutely different species, of which one happens to be naturally susceptible and the other naturally refractory, they may be rejected at once.

(1) Those who object to test-tube experiments as being artificial, do not hesitate to use little paper bags filled with germs, and place them under the skin of a refractory or immunised animal. Such experiments are as little natural as test-tube researches, for (*a*) we thus localise the process artificially; (*b*) the fluid which passes through the filter-paper may be of an inflammatory nature, and is not necessarily the same as the normal body fluids. For this reason I have not before alluded to Sanarelli's experiments, who showed by using collodion tubes that the lymph of frogs *in corpore* can attenuate or even kill anthrax bacilli without the aid of phagocytes.

(2) Waiving, however, this objection for argument's sake, Dr. Ruffer claims to have disproved the protective influence of the living plasma by his latest experiments. He placed the vaccine of charbon symptomatique wrapped up in paper under the skin of an immunised rabbit, and found that even after forty-eight hours the vaccine with certainty killed guinea-pigs. This to my mind proves

nothing, for it is not at all necessary that the plasma or body fluids of the immunised rabbit should kill or attenuate the bacillus; the animal will survive as long as the poison is destroyed, and the immunisation of the rabbit may simply have enabled the organic fluids to do this. The fact that the exudation was able to wash away a part of the metabolic products of the bacilli secluded in the paper can only be of advantage to the growth of the same.

It may be mentioned, in passing, that claiming such powers for the organic living fluids as I have done does by no means imply a retrogression to the ancient humoral pathology; for no one, I take it, denies that all our fluids are the products of cellular secretion or excretion—and this is all that cellular pathology demands.

In studying the artificial production of immunity the absolute followers of Metschnikoff are prone to neglect the most important part in the causation of infective diseases and lesions, viz. the chemical products of the microbes which undoubtedly cause the phenomena of such diseases.

(*a*) We find that an animal, made immune against a living microbe, can also resist the toxine of such microbe to varying degrees. Examples are tetanus, pneumonia, diphtheria, *Vibrio Metschnicovi*, *pyocyaneus*, charbon symptomatique, and others.

(*b*) *Vice versâ*, an animal made immune against toxine also resists the living microbe. Therefore the processes responsible for these results must assumedly be the same. Now immunity against toxines cannot in any way whatever be explained by means of phagocytosis.

I conclude, therefore, that at the present state of knowledge it is impossible to assert that the living plasma (and body fluids) are of no consequence. I will not claim more for the present.

II. *Chemotaxis* has of late been introduced as a welcome support to the phagocytic theory. Certain chemical substances, according to their degree of concentration, attract or repel phagocytes; but if the latter are in a medium already containing these chemical substances, equally distributed, they will not be attracted on adding more of these substances unless they be added in a highly concentrated condition. According to this doctrine we have three possible cases:

(*a*) The metabolic products of the microbe are present in equal quantity in the tissues and at the seat of lesion—therefore no migration of phagocytes can take place.

(*b*) If the degree of concentration is higher at the seat of lesion, we must have a migration of phagocytes thereto.

(*c*) If the degree of concentration is higher in the blood, the phagocytes may migrate back into the blood.

This teaches us nothing as to the acquisition of immunity: for if true, (1) it is simply a statement of concomitant facts; (2) on such a view our successes in the production of immunity become merely a matter of chance and good fortune; (3) it supposes, without the slightest foundation, that in an animal immunised against a microbe the toxine of such microbe circulates in its vessels; and lastly, it neglects the fact that besides diapedesis we have, as a rule, hand in hand with positive chemotaxis a great general increase of phagocytes and leucocytes, depending of necessity on a stimulation not only of the leucocytes or phagocytes themselves, but also of the elements giving birth to these bodies. Hertwig in his monograph sums up this theory thus:—(*a*) "In an immunised organism the negative chemotaxis, which the body exhibited before being made immune, has been replaced by a chemotaxis behaving positively towards the specific virus." If so, we ask "why and how?" We are also told that (*b*) "the effects of the metabolic products of microbes show themselves as positive and negative chemotropism, and also as acquired irritability (*Reizmachwirkung*). The existence of positive chemotropism explains the localisation of the virus through the attraction of leucocytes and subsequent phagocytosis. The existence of negative chemotropism explains the possibility of a general infection by means of a diffusion of the micro-organisms. By means of suitable injections of bacillary products a negative may be changed into a positive chemotaxis, and thus a cure be effected." This is mystical and unsatisfactory, and treats of the body as though it were a specimen on the microscopic slide.

III. We now come to the last point, *phagocytosis* itself. I repeat that I fully acknowledge that this exists, and also that it is an important phenomenon during and after the acquisition of immunity, but I am far from accepting that it is the sole or even the chief factor, active in all cases alike. The exclusive phagocytic theory is both inadequate and unsatisfactory. I will not here repeat the classical objections which are always answered by the same classical arguments, but shall enumerate a few difficulties as they have presented themselves to me.

(1) By causing fever artificially in a susceptible animal, two to three hours after the temperature has begun to rise considerably there is a great increase of leucocytes, not only of the so-called lymphocytes, but also of the larger element, and this leucocytosis persists for more than twelve hours. On inoculating the animal, when in this condition, with anthrax, it will die just as usual. Yet here the army of leucocytes was increased at least tenfold.

(2) Hence the increased number of phagocytes *per se* is not sufficient. They require also the special training. And here we come to the most unsatisfactory part of the theory. Before an animal is immunised the phagocytes are more or less inert against a particular microbe, but as soon as ever a relative immunity is established they are extremely voracious. We must ask why does phagocytosis appear now, and why are the cells suddenly enabled to destroy what previously perhaps killed them? Metschnikoff says "by means of a special selection or change of habit." This to my mind amounts to saying that the cells themselves have acquired immunity, and phagocytosis, instead of explaining the process by which immunity is acquired, becomes simply a phenomenon observed during or after the process.

We must also remember that in many cases after the protective inoculation we have to wait from four to sixteen days before immunity is apparent, and during this time the natural resistance may even be decreased, as Frænkel's experiments on diphtheria immunity show. Leucocytes and wandering cells are but short-lived, and, as far as we know, largely replaced through continuous division of cells which form the elements of certain tissues and organs. Thus the assumed hereditary resistance must be sought at the birthplace of these leucocytes and wandering cells. If we allow so much, we might as well say the phagocytes are immune because the whole body has become immune, or simultaneous with immunisation of the organism phagocytosis appears.

(3) The occurrence and importance of vaccine fever during the process of immunisation points to more general changes than a mere change of habit of the phagocytes alone.

(4) That changes exist in all the tissues has been shown by Emmerich, who succeeded in protecting animals by inoculating them with the tissue juices of immunised animals.

(5) Some of the methods of immunisation, as the injection of so-called antitoxines, or of small repeated doses of poisons, &c.,

point strongly to general changes in the body, the phagocytes being altered with the rest of the body.

(6) Lastly, phagocytosis does by no means explain many of the phenomena mentioned in the first part of the discourse. Other objections might be raised, but I am afraid I have already trespassed on your patience.

In conclusion, it seems to me that we cannot hold any one process exclusively responsible for the artificial production of immunity. The primary cause of immunity, however, must be sought beyond the leucocyte or phagocyte, and also beyond the fluids of the body, and according to the maxims of cellular pathology depends on changes in the cell life of the organism which at present we are unable to understand. It is in consequence of these as yet obscure molecular changes that phagocytosis and the other phenomena observed after or during immunisation appear, but none of these alone can be considered the cause or explanation of immunity.

Dr. J. S. Bristowe.—The subject of immunity in relation to diseases due to the invasion of living organisms is one of surpassing interest, and one on which I have bestowed a good deal of thought. But I have never worked at it systematically, as many of you have done and are doing, and cannot therefore claim to be much more than an amateur in the matter, or to have the right to dogmatise. Still, having been honoured with an invitation to take part in the present debate, I have thought that I might without impropriety accept it; and I trust that, under the circumstances, I shall be forgiven if the views I express are somewhat commonplace, and scarcely up to date.

It seems to me that, looking at the question of immunity from a somewhat different point of view from that in which it has been regarded by the speakers who have preceded me, there are three different forms or phases of it which call for investigation. The point to which hitherto the discussion has been practically limited concerns the means by which the living organism protects itself against invasion. The second relates to the spontaneous arrest or to the cure of infectious diseases. The third has reference to the immunity or protection which the attacks of some such diseases confer against subsequent attacks of the same diseases.

(1) It has long been recognised that the causative organisms of infectious diseases have more or less difficulty in gaining entrance into the living body. The skin, and in a less degree the mucous membranes, constitute mechanically protective barriers. But they are not uniformly protective, and there are some parts of the skin, and especially some parts of the mucous surfaces, such as those of the tonsils and fauces, of the bronchioles and of Peyer's patches, which are highly vulnerable; and, further, as we all admit, abrasions and various pathological changes in these parts diminish their protective capacity, or even invite attack. But even when the invaders are in process of penetrating, or have actually penetrated, these membranes, they have not necessarily conquered. In some cases, by exciting local irritation or inflammation, they become checked in their progress, or, it may be, surrounded (as a bullet or other inert body often is) by a barrier of inflammatory lymph. In other cases, as has been well shown, and as I do not hesitate to believe, the leucocytes and other elements of the living tissues, attracted to the breach, enter into active warfare with them, and wholly or in part eat them up or perish, as the case may be. It must also be allowed that there may be incompatibility between the invaders and the sanitary circumstances in which they find themselves: the soil may, so far as they are concerned, be sterile, the food and other conditions of life may be unsuitable, or they may be exposed to the malign influence of poisons, either originating in the invaded organism or secreted by their overcrowded selves. It seems easy to understand how by such means, acting either singly or in combination, their hostile proceedings may be neutralised or arrested, and they themselves repulsed, imprisoned, or destroyed.

But, notwithstanding such obstacles, certain of the invaders may pierce the first line of defence, and find themselves in the spaces of the connective tissue; or even, in some cases, the invaders may gain entrance without encountering any material opposition. In either such case, again, there may be local warfare; but some will probably find their way into the lymphatics or blood-vessels. If they find their way into the lymphatics they are carried with the lymph to the nearest lymphatic glands, where the conflict is probably resumed. Here, again, the invaders may, after doing more or less local mischief, be routed, or in other ways arrested in their onward march; or, on the other hand, they may seize the citadel, may flourish and multiply therein, and, after a longer or shorter

time, emerge thence, reach the blood-vessels, and through their agency become distributed over the organism to take up their abode or to work havoc in those tissues or those organs which are most defenceless or are richest in the necessaries or luxuries of microbe life. If they find their way primarily into the blood-vessels, the general distribution of them or of their products (unless this be checked by some one or other of the processes which have already been considered) takes place at once.

(2) That many of the infectious diseases tend to run a definite course, ending in spontaneous cure, is a very remarkable and interesting fact. It might well, in the absence of experience and on theoretical grounds, have been supposed that, in the case of diseases due to the dissemination and multiplication of poisonous microbes throughout the organism, the natural tendency would be to the persistence and progressive aggravation of the malady to its culmination in the death of the patient. In some cases, no doubt—as, for example, in tuberculosis, in leprosy, and in syphilis (which, in this respect, are closely related to cancer),—such is the natural tendency; yet even here we find that, while the disease is still progressing, local outbreaks are not infrequently arrested or suppressed, and that occasionally the simultaneous or repeated defeats of local outbreaks result in a substantial cure. In diphtheria, in typhoid fever, and in epidemic cholera there is reason to believe that the specific morbid organisms flourish mainly, if not exclusively, at the seat of inoculation, causing serious local mischief; while the general symptoms are due wholly or in chief part to the absorption and general distribution of poisons locally manufactured. In such cases the cure of the disease means the subsidence or the cure of the morbid process going on in the part primarily affected. In the exanthemata, and in certain other maladies which are obviously related to them, the conditions of cure are apparently altogether different from those which characterise the classes of disease hitherto considered. For here the morbific organisms, as in tubercle, actually invade the system, and swarm either generally or in certain tissues and organs; but then, after having inflicted more or less damage (which may, of course, be so great as to prove fatal), and at the end of some definite period, tend to die out or to become discharged, and thus to leave the patient free and convalescent. The very facts that such diseases run a specific course, and that their natural tendency with few exceptions is towards

recovery, implies that in some way or other their occupation of the body involves their ultimate overthrow, and brings immunity. How this result is attained has never yet been satisfactorily explained, and remains a mystery.

(3) Probably the most interesting fact, as it certainly is one of the most important practical facts, in connection with the infectious diseases, is the immunity which, in many of them, one attack confers against subsequent attacks of the same disease. As I have already hinted in the last paragraph, the fact that a generalised infective disease after a certain definite course gets well spontaneously is a proof that immunity has been produced; for were it not so, the multiplication of morbific organisms in the body, instead of being suddenly and completely arrested, would still go on in geometrical progression. But how long or in what degree immunity shall be maintained is another question. We know that in some cases the acquired immunity appears to be lifelong and absolute, that in other cases it tends in the course of time to become impaired and to die out, and that persons are occasionally met with in whom acquired immunity against some one or more of the diseases under discussion is habitually imperfect and of short duration. The diseases which are truly self-protective seem to be those only, of which the contagia after inoculation are distributed throughout the body, multiply therein, and then spontaneously die out. There is much reason to doubt whether—and I do not myself believe that—diphtheria, typhoid fever, or epidemic cholera is self-protective in the same sense as is measles or smallpox. Ague is not self-protective, nor are the ingravescent infectious diseases, tubercle, leprosy, syphilis, and cancer; nor, again, are septic diseases. I may here repeat that the question of immunity appears to me to be involved in the question of spontaneous cure, and to neither of them as yet has any adequate, or, in my opinion, even plausible solution been offered.

I propose now to discuss the pathological phenomena of several typical diseases which have been above alluded to, with the object of showing in what respects they resemble and in what they differ from one another in their natural history, and of indicating incidentally what, if any, light is thus thrown upon their behaviour in regard to the limitation or diffusion of infection and to spontaneous cure.

(1) Small-pox in a particularly interesting and instructive dis-

ease, because of its striking characteristics, of the fact that it can be readily imparted to susceptible persons either by direct inoculation or by the inhalation of its virus, and of its relation to cowpox. When smallpox is inoculated, say upon the arm, there arises, at the point of inoculation, a pimple which develops into an umbilicated pock and attains its maturity on the eighth day. While this is in progress one or more of the glands in the corresponding axilla undergo progressive enlargement. On the eighth day after inoculation the symptoms of invasion suddenly declare themselves, and on the second day thereafter the general eruption first appears. Now each pock of this eruption undergoes the same successive developmental changes, and presents the same characters as did the pock resulting from direct inoculation; and there can be no reasonable doubt that these also are the result of direct inoculation, but of inoculation by the virus carried to the skin by the blood vessels at or about the time of the so-called invasion. From these, however, there is no reinoculation of the system. When they subside or are cast off the disease comes to an end. In the case of smallpox acquired in the ordinary way, that is by the inhalation of its virus, the resulting phenomena are essentially the same as those which have just been considered. But there are these differences: no pock, so far as we know, results from the inoculation of the respiratory mucous surface, and the period of incubation, or the time that elapses between the exposure to the virus which causes the disease, and the occurrence of invasion is twelve instead of eight days. It is clear, of course, that the time during which the inoculated pock is attaining its maturity corresponds to the period of incubation of the natural disorder. But why, it may be reasonably asked, does the incubation in the one case occupy twelve days, in the other only eight? The explanation doubtless is that in the natural disease delay is occasioned by the fact that the virus experiences some difficulty in overcoming the resistance opposed by the uninjured respiratory mucous membrane. Whether or not any evidence of the warfare, that it may be presumed has been going on, exists and might with careful examination be discovered in some part or other of the respiratory tract, I do not know. The phenomena presented by the inoculated disease would lead one to believe, that some of the virus introduced at the seat of operation finds its way into the lymphatic vessels, and thence to the lymphatic glands in connection therewith; that in these it is

detained and undergoes development, until after a definite period (corresponding to the period of maturation of the primary pock) it is shed thence in showers which find their way into the veins, and are, by their agency, distributed throughout the organism to take root and undergo further development in the skin and such other tissues as furnish a suitable soil.

(2) The sequence of phenomena in syphilis has a close resemblance to that in inoculated smallpox. The immediate results of inoculation are the development of a chancre, and the involvement of the lymphatic glands next above. These are followed, at the end of a few weeks, by febrile disturbance and other evidences of the generalisation of the disease. It is obvious that the chancre and affection of the lymphatics correspond to the early phenomena of inoculated smallpox, and that the early symptoms of generalisation correspond to those of the invasion of smallpox; and it may reasonably be assumed that these latter symptoms are due to the dispersion, by means of the blood-vessels, of the virus that has accumulated in the affected glands. The further progress, however, of syphilis is very different; for, instead of undergoing spontaneous cure, it tends, in an ever-increasing but fitful and irregular manner, to perpetuate itself by local outbreaks of which many during its progress, become arrested or die out.

(3) Tuberculosis has some affinity to syphilis, and some perhaps to smallpox, but differs in many important respects from both. It is largely a local disease, but it has a marked tendency to become generalised, and in a large proportion of cases, becomes generalised. If it be contracted in what is probably the usual way, namely by inhalation, it affects the air passages, and as a rule the terminal portions, in the first instance, producing the ordinary form of pulmonary phthisis; and after a time probably it becomes complicated by tubercular disease of Peyer's patches, due to swallowing the infected sputa, and consequently to direct inoculation of the vulnerable parts of the bowel. But it also leads to secondary involvement of the mediastinal and mesenteric glands, and hence to more or less general diffusion of the tubercular process throughout the body. In the case just referred to the local processes arising from direct inoculation are, as a rule, the most important; but in the condition known as general tuberculosis, we find a rapid and almost simultaneous general development of miliary tubercles. And in many such cases there can be no doubt that the starting-

point of the affection is (as one sees in the experimental production of general tuberculosis in the lower animals) some comparatively trivial and inconspicuous local tubercular development; from which (as in smallpox) swarms of bacilli are directly, or indirectly through the lymphatic system, shed into the venous circulation and so distributed. On the other hand, it is very interesting and instructive to note how tubercle inoculated on the skin will remain limited to the skin for years or for life without infecting the general system; how tubercle affecting the glands in the neck, and causing suppurative destruction of them, will in many cases cause no further mischief; and how, again, the same phenomenon may be observed in connection with tuberculosis of bones and joints. It is further interesting to observe that in tubercle, as in syphilis, a patch of disease may remain quiescent, or even undergo degeneration, and yet after a time prove the starting-point of a secondary and may be wide-spread diffusion.

(4) Diphtheria may be taken as the type of another kind of infective disease. In this, as I have before observed, the primary lesion is usually the most important item in the biography of an attack. It is here that the specific organism implants itself and spreads in depth and in surface, leading to the production of a false membrane, and to inflammation of the subjacent tissues and of the neighouring lymphatic glands; while the symptoms referrible to the rest of the organism are mainly, perhaps solely, due to the absorption thence of poisonous matters. One reason for hesitating to accept the view that in this particular instance the remote symptoms are wholly due to absorbed poison, and in no degree to the diffusion of microbes, is that the characteristic paralysis so often comes on some weeks after all evidence of local disease has disappeared. But, however that may be, it is certain that all the local processes of diphtheria correspond to the inoculated pock of smallpox, and not to the generalised disease which begins with the symptoms of invasion.

(5) The last affections to which I shall advert are the so-called septic disorders. I shall not presume to offer an opinion as to whether, or in what respects, these affections differ specifically from one another. It may, of course, be that the differences to which I propose to call attention are due wholly or in part to specific differences in apparently allied contagia; it may be that they are wholly or in part due to different conditions connected with the

parts or the persons attacked; but, at any rate, they are interesting, and they have their counterparts among the various affections that have already been discussed. Assuming that an accidental wound becomes infected with septic organisms and takes on unhealthy action, what follows? In some cases the organisms (as also in diphtheria and in tetanus) multiply only at and in the neighbourhood of the seat of inoculation, and the general symptoms of disease are the result of the absorption of the poisonous matter locally produced, and not of the invasion of the system by the organisms themselves. This affection has been called septic poisoning. In some cases the organisms, besides flourishing locally, find their way into the lymphatics, and lead to inflammation in their course and in the corresponding lymphatic glands, and probably also to abundant suppuration. This accords very much with what we observe in the early stage of inoculated smallpox, and in tuberculosis culminating in suppuration of the glands of the neck. In some cases, again, the microbes enter the blood-vessels at once, rapid generalisation takes place, and the phenomena of septicæmia or pyæmia declare themselves. It is interesting, however, to observe how, even in the case of septic infection tending to become generalised, there is a tendency for, at any rate, the coarser processes of disease to be limited to some one section of the circulation; how in ordinary cases of pyæmia these are often limited to the venous circulation, and mainly therefore to the lungs; how in ulcerative endocarditis they tend to be confined within the arterial circulation, and hence to leave the venous circulation and the lungs unaffected; and how, finally, in so-called suppurative pylephlebitis the pyæmic phenomena tend to be circumscribed within the portal circulation. Of course in each of these cases septic poison, or even septic organisms, may extend beyond these comparatively narrow limits, and the system suffer generally; and it may even be that the pyæmic phenomena themselves become more widely distributed.

In conclusion, I propose to make a few remarks suggested by the foregoing discussion.

1st. It is obvious that the more serious and striking phenomena of infective diseases do not in all such diseases occur at a corresponding period in their progress. Thus, in cholera, typhoid fever, or diphtheria it is the morbid process going on at the spots of inoculation, and the symptoms that are caused thereby, that con-

stitute mainly the disease as we know it, and are the special sources of danger. No doubt in each of these cases symptoms arise later, either connected with the entrance of organisms into the system, or due to the simple absorption of poison. And in the case of diphtheria these later symptoms form a very distinctive feature of the malady. But in smallpox and the true exanthemata, and in whooping-cough, mumps, and the like, the phenomena due to the process of inoculation are almost or quite unappreciable; and it is only when the morbid processes become generalised (that is, after a period of incubation which is different for each affection) that the symptoms of the diseases as we understand them come on suddenly and then run a definite course. It is clear that in the former group of diseases we have no period of incubation corresponding to that characteristic of the latter group. In tuberculosis the phenomena due to the primary local disease, as it occurs for example in the lungs and in the skin, are as striking and as characteristic as are the phenomena which attend its generalisation, or, in other words, the development of general miliary tuberculosis.

2nd. In considering the fact that, although the pocks of generalised variola originate in inoculation from the blood, and are centres for the development of virus, they never reinfect the system, it has seemed to me probable that this phenomenon is due to the development of a protective inflammatory barrier between each one of them and the surrounding living tissues. But if this be a correct view of the case, it would seem to follow that the same thing occurs in relation with the primary inoculated pock, and that what happens when the virus is implanted in the skin is that a portion of it takes root locally, so to speak, and produces a crop which has no influence on the organism, while another portion is taken up by the lymphatics, and finds its way into the glands, whence at the time of maturation it is shed into the blood. A further argument, as it seems to me, in favour of this view is furnished by the suddenness of the symptoms of invasion. For if the virus in process of manufacture at the seat of inoculation were during the whole period of the appearance of the pock being shed into the system, it is difficult to see why the period of invasion should be long delayed, and finally of sudden onset. This view suggests that in the case of cow-pox also the inoculated virus is used up partly in forming a local pock, partly in infecting the neighbouring lymphatic glands, and that it is only the latter

portion which brings about the general infection of the system and gives protection against smallpox; and it suggests further that, if the cow-pox virus were inserted deeply by means of a suitable syringe, it might cause the glandular affection and the general infection without the production of a pock, or, indeed, of any obvious local malady.

3rd. I fully admit the great value of the knowledge which has accrued from recent inquiries into the subject of phagocytosis and the production of poisons by morbific organisms; I unhesitatingly believe that it throws a very important light, not only on the processes of infection, but also on the methods by which the invaded body resists attack; and I think it highly probable that those who are working at these subjects are on the trail of valuable and far-reaching discoveries in relation to the pathology and treatment of infective diseases; but I am not prepared to admit that it has yet been shown how it is that certain kinds of infective diseases run a definite course tending to end in recovery, and how it is that in these same diseases one attack confers immunity against subsequent attacks of the same disease. It must be allowed, however, that these latter questions are very obscure and very complicated; for the more closely one considers the different kinds of infective diseases, the more clear it becomes that, although they fall into several fairly well defined groups, they are individually quite distinct from one another, and their contagia are severally endowed with distinctive habits and distinctive qualities, and that hence, notwithstanding apparent resemblances, there is good reason to suspect that the causes of spontaneous cure and the causes of immunity may be very different in different (even though apparently allied) cases.

Dr. William Hunter.—Let me at the outset recall very briefly a few of the facts to which attention has already been drawn in detail by Dr. Woodhead in the address with which this discussion has been so ably opened.

I.—Facts relating to Immunity.

The facts, then—to take the simplest case—are briefly these: that in non-protected animals virulent bacteria inoculated subcutaneously produce little or no local change, grow unhindered, and

cause general infection; while in protected animals inoculation of the same bacteria is followed by a local leucocytosis at the point of injection, a certain degree of inflammation is set up, and general infection is prevented.

In virtue of some change in the body, that which was formerly capable of setting up a general disease, can now only set up a local affection. What is the nature of this change? On the one hand, we have the bacteria, with their powers of forming poisons, undoubtedly capable in many instances of affecting the organism most injuriously. These poisons are of two kinds: (1) easily diffusible substances of alkaloidal nature—toxines—whose mode of action on the organism is analogous to that of the vegetable alkaloids; and (2) less diffusible substances of proteid nature, whose nature is still very imperfectly known. So far as is known, however, their action resembles more that of ferments than of ordinary chemical poisons, inasmuch as it is lost on heating to a temperature of 50° or 60° C., at which the active properties of ferments generally are destroyed. Both these classes of poisons stand in the same relation to the bacteria, in so far as they are the special products of their activity, in the same way that nitrogenous products such as urea, or active proteid substances such as ptyalin or pepsin, are the products of the activity of cells of higher organisms.

In addition to these two groups of metabolic products formed by bacteria, there is another class, differing both in origin and action from the foregoing. These are also proteid bodies, having, so far as is known, the character of albumoses. These are substances—first described by Nencki in 1880—derived from the bodies of the bacteria themselves, so-called "proteins," for a knowledge of whose action we are indebted, perhaps, most of all to Buchner. They resist in a remarkable way the action of heat, withstanding when in a moist condition even boiling temperatures. Their most remarkable property, however, is their chemotactic power, the power of attracting wandering cells, and of inducing, therefore, a greater or less degree of leucocytosis wherever they happen to be present. Their action in this respect I hope to illustrate to you later on.

It is to be noted as a further difference between these two classes of bacterial products, the toxines and toxalbumins on the one hand and the proteins on the other, that the former are only

formed, and are formed most abundantly, when the bacteria are active, the latter only, and most abundantly, when the bacteria are dying.

A further difference—an important physiological one—may be noted, namely, that while the former are responsible for the general symptoms of disease, the action of the latter is, in the first instance at least, mainly a local one. Without being entirely confined to the part where they are formed, the most important action of these proteins, and the one which lends them their chief interest, is the chemiotactic power above mentioned.

When we turn now from the invading bacteria to the organism thus attacked, we find that the means it has at hand to defend itself are of a twofold character. On the one hand, there are the cells—especially those free lances of the body, the wandering leucocytes—having the power of seizing upon everything, animate or inanimate, possessing a less power of resistance than themselves, and, in virtue of this power, doing undoubtedly much useful work for the organism both in health and disease. The theory of phagocytosis, so beautifully and skilfully elaborated by Metschnikoff in the first instance, assumes, on the basis of many observations whose accuracy cannot be seriously called in question, that this power is exercised in a special degree by the cells in defending or protecting the organism against bacteria.

This is admittedly, however, not the only weapon possessed by the body in its defence. Apart altogether from the action of living cells, the plasma and serum of the blood is now known, through a series of equally beautiful researches, to possess, under certain circumstances, antibiotic properties when withdrawn from the body, bacteria being killed after a short exposure to their action.

It has been shown, moreover, for certain bacteria (for example, *vibrio Metschnikovi*, by Behring, and Nissen) that the power which the body possesses of resisting their action is proportional to the antibiotic properties of its blood-serum, the serum of animals rendered immune having strong bacteria-killing power, while that of the ordinary animal favours the growth of the bacteria. This, then, is the basis of the view opposed to the phagocyte doctrine, of the so-called humoral doctrine. It is assumed by the upholders of this view that the protecting power possessed by the body is really due to these antibiotic properties of blood-serum—to the action of the fluids of the body rather than of the cells.

Unfortunately for this view, which, in presence of such facts as those above referred to, seems a reasonable, not to say a seductive one, it is admitted that this relation between degree of protection possessed by the body and the antibiotic properties of its blood-serum is not only not constant, but that in certain cases it is completely reversed, and that the serum of an animal very sensitive to the attack of certain bacteria when these are injected into the body, may be nevertheless extremely bactericidal in its action on these bacteria when tested outside the body. Thus it has been shown by Roux and Metschnikoff that the serum of young rats sensitive to anthrax has a bactericidal action on anthrax bacilli outside the body; and by Lubarsch that the extravascular blood of a rabbit can kill millions of anthrax bacilli, while a few of these injected into the blood suffice to kill the animal.

It is clear then that some caution is necessary in deducing from the action of blood-plasma and blood-serum after it is withdrawn from the body what its action within the body is likely to be. So far as the evidence at present goes, there is, in my opinion, no established relation between the two.

As regards the nature of the substance or substances in plasma or serum to which this bactericidal action is due, little is known further than that they are proteids. In one case the substance was found to have the characters of globulin (Hankin), but with this exception—and the observation is an isolated one—but little progress has yet been made in identifying these substances with any special class of proteids. The most recent work renders it to my mind exceedingly probable that it is not to any one definitely characterisable proteid substance that this bactericidal property of serum is due, but rather to some special association, of an altogether more complex character, of one or more proteids.

The recent work of Dr. Wright, on which, I trust, we may hear something from him in this discussion, appears to me to have a special interest in this relation, and a very direct bearing on this point.

He has shown that the "tissue fibrinogen," to which Wooldridge ascribed such an important *rôle* in coagulation phenomena, and which he found also to be capable of conferring a certain degree of protection against anthrax, is, in all probability, a double proteid body, one of albumose nature, and the other a nucleo-albumin.

II.—Interpretation of these Facts.

So much, then, for the facts on which, as Professor Sanderson has said, we are for the most part agreed, and so much incidentally for certain of the difficulties that arise in interpreting aright their significance. If we now consider the application of these facts to the phenomena of acquired immunity, as above described, we find that the divergences of opinion which exist among bacteriologists relate more to the order of occurrence and relative importance of the events than to the events themselves.

The two chief events are that a short time after the inoculation of virulent bacteria into an immune animal a large number of leucocytes are found at the seat of inoculation, and a large number of the bacteria are found lying enclosed within these leucocytes and other adjacent cells.

According to the doctrine of phagocytosis, the leucocytes have been attracted thitherwards by the chemiotactic action of certain of the products of bacterial action; and they then act as phagocytes, and engulf the bacteria. So far as I can understand, it is not denied that in "reacting" to the presence of these products they may likewise produce substances capable of acting on the bacteria injuriously outside the cells. It is nevertheless maintained that the intracellular method is the chief method employed in injuring the bacteria. The protein substances given off by the dying bacteria exert further chemiotactic action, and attract more leucocytes, till finally, at the seat of attack, is mobilised a regular army of agents capable of resisting successfully all further invasion.

The opponents of this view maintain that the first event is not an attraction of leucocytes, but a death of certain of the bacteria brought about through the agency of the bactericidal substances present in the serum, and that the leucocytosis is secondarily induced by the proteins set free from the injured bacteria. The subsequent inclusion of the bacteria within these cells is an event of altogether secondary importance. The cells in taking up the bacteria, exercise merely their ordinary scavenging function, and not any special phagocytic function.

The question at issue between the two opposing schools is thus one that lends itself readily to active discussion, for the differences between them are those of degree rather than of kind.

The upholders of the phagocyte doctrine assert that their opponents attach too much importance to the bactericidal action of blood-serum, and too little to the cells; while the latter retort that the so-called phagocytic function is a purely scavenging function, and that the chief factor in inducing the leucocytosis is the production of proteins from the already dying bacteria.

In the words of Buchner, the chief exponent of the humoral theory, the essential active processes underlying immunity can only be of chemical nature. According to him it is a fatal error to assume that in protected animals the bacteria find themselves in precisely the same conditions, before leucocytosis sets in, as in non-protected animals. According to the doctrine of phagocytosis, on the other hand, it is the special reaction of cell protoplasm that determines the issue, the action of chemical products being of secondary importance. A certain antagonism there undoubtedly, therefore, is between the two views, but the doctrines are not in my opinion so opposed to each other as to be mutually destructive.

I gather from the course the discussion has so far taken that some misapprehension seems to exist on this point. It is assumed that there is an inherent antagonism between the two views, and that to establish the one it is only necessary to demonstrate the weakness of the other. Acting on this assumption, the speakers so far have confined themselves mainly to pointing out in how far the doctrine of phagocytosis falls short of perfection. The result has been to show that in their opinion it falls very far short indeed of that point, for we have heard that not only is it imperfect, as we all admit, but that it is utterly opposed to general biological principles; much of it untrue; what of it is true is not new; it is illogical, mechanical, in fact altogether unsatisfactory. Having made out this case to their own satisfaction, the speakers appear to think that they have firmly established the immense superiority of the opposing view.

Their practice appears to be based on one, if report speak true, not altogether unknown at the bar, which consists in supporting a case, itself weak, by exposing the weak points of the one opposed to them. In the present instance it takes the form of abusing the doctrine of phagocytosis, and letting judgment go by default in favour of the "humoral" doctrine. They have unconsciously accepted a brief for the latter doctrine, and have done their best for their client by abusing the opposing one.

Objections to the doctrine of phagocytosis.—The objections raised in this discussion against the doctrine of phagocytosis group themselves into two divisions: (1) General, those which impugn the inherent probability of the doctrine, charging it with being mechanical, illogical, opposed to biological principles; and (2) special, those which dispute the accuracy of the data on which it is based.

(1) *General objections.*—With regard to the more general objections, it is extraordinary how much opposition has been called forth by this doctrine, and how much warmth of feeling has been imported into the controversy that has been raised around it. It is little wonder that outside witnesses of the controversy should conclude that some deep underlying principle must be at stake, and that the two views must be utterly opposed to each other.

What then are the principles involved? On the one hand, it is asserted by the upholders of the doctrine of phagocytosis that living cells have the power, under certain circumstances, of taking up living bacterial organism; of acting on them in such a way as first to kill them and then completely destroy them.

In other words, it is asserted that one form of living protoplasm has the power of taking up within itself another and presumably weaker form and destroying it altogether. It appears to me that if any biological principle is more firmly established than another, it is that such a power is possessed by protoplasm. It is maintained further that this is the chief way in which the body protects itself against attacks of infectious disease, and that the difference between one who has had an attack of an infectious disease—for example, scarlet fever—and has thereby acquired protection, and one not so protected, is that in the former the individual cells have acquired some additional property, that enables them to resist successfully from the beginning where previously they had only been able to do so after the disease had run a certain course.

As thus put, the doctrine seems to lay itself open to the charges brought against it: that it does not add much to what we previously knew; that it only expresses in terms of the cell what we have long been in the habit of stating equally clearly in terms of the body as a whole; moreover, that it brings no new properties of the cell to light, for that we have long known that cells had a sort of scavenging function, and were in the habit of taking up, so to speak, whatever they could lay hold of.

In reply to these various objections, it may be I think urged that,

even if it had only directed our attention from the body as a whole to processes going on in the individual cells of that body, an important step would have been taken—a step in the direction in which all advance in pathology has been, and is destined to be, made—namely, from the general to the special. The history of pathology is a history of such advance, from the spirits which formerly caused disease, independent of the body, to the body itself; from the body as a whole, with its vapours and humours to the particular organs involved; from the organs to the special cell structures implicated; from these in turn to the nature of the disturbing cause. Further, that while it is not claimed that any new property of cell protoplasm has been discovered, the observations on which the doctrine of phagocytosis is based are an important extension of our knowledge of cell function in an entirely new direction. It is the application of the teachings of cellular pathology to the phenomena of infectious disease and immunity from that disease, and to that extent it can fairly lay claim to have added something new to our knowledge.

And when we come to the question of logic, which position is the more logical—that which ascribes to cell protoplasm and direct cell action, as the doctrine of phagocytosis does, or that which ascribes to certain products of that activity acting at a distance from the cell, as the opponents of that view maintain, the power of combating and ultimately destroying pathogenic micro-organisms? I confess for my own part I have little hesitation in giving my opinion.

And it is this, that the view which ascribes to products of cell action present within serum or plasma the property of being able successfully to wound, maim, and render harmless invading bacteria, and yet denies to the protoplasm of the cells which produce them the slightest power of controlling or in any way influencing the growth or virulence of bacteria. Such a view, I submit, is as utterly illogical as any could well be.

On grounds of logic I give decidedly the preference to the view which subordinates the product to the cell which produces it; and hence, if I have to choose between the phagocyte theory which exalts the direct action of the cell without ignoring its more indirect action, and the humoral theory which exalts to a pinnacle the action of bactericidal substances admittedly produced by cells, while

denying to these same cells any special bactericidal action, I give my decision unhesitatingly for the doctrine of phagocytosis.

2. *Special objections.*—The above does not constitute, however, the head and front of the offending of this doctrine in the eyes of its opponents. That which above all appears to them as gratuitous foolishness in it is, I take it, that it not only ascribes to cells, but to certain particular cells, this special phagocytic function. It is this pretentious claim on behalf of the leucocyte and lymphocyte that rouses the special scorn and indignation of the humoralists; and they express a contempt for these little structures that, could they but feel it, would cause them to shrivel up with shame at their own want of modesty, and general aggressiveness of conduct towards bacteria.

Curiously enough, it is this special claim of the phagocyte theory, when considered in relation with the facts on which the humoral theory is based, that commends it specially to my acceptance, and strengthens the probability of the view for which it contends, that the duty of defending the body against the attacks of infectious disease is not distributed amongst the cells of the body as a whole, but is relegated to certain special cells. These are arranged so as to constitute what has been termed two lines of defence. The first line of defence is formed by the leucocytes of the blood; the second by the lymphocytes and of follicular tissue generally, chiefly that of spleen. The former bear the first brunt of the attack at the seat of inoculation, the latter act as reserve forces.

According, then, to the doctrine of phagocytosis, acquired immunity is due to an altered habit of body on the part of these cells, transmissible from generation to generation. Its opponents, scorning such a view as visionary and unsatisfactory in the extreme, and based on insufficient data, prefer to refer it instead to a change in the character of the fluids of the body.

Now I would point out that this latter view implies an altered consitution on the part of the plasma and serum of the blood, without even suggesting in what way such an alteration has been brought about, except through the agency of cells.

Moreover, this alteration is one that in certain cases presumably lasts for years, and hence one of two conclusions follows; either that, once produced, it remains permanent—that blood plasma can transmit its characters without the intervention of cells; or that the change is one constantly being carried out by the cells of the

body. The former, I need hardly say, is a wild hypothesis, having no support either in facts or analogy; and therefore we must except the alternative conclusion that, *even on the humoral theory of the nature of immunity, the essential change is an alteration in the cells, such as the doctrine of phagocytosis contemplates.*

This, however, it may be urged, does not carry us very far forward. We knew before, as Professor Sanderson has already pointed out, that the body possessed what he has termed a specific power of resistance to disease; and this *vis medicatrix naturæ* is naturally derived from its cells, if not resident in them.

The final teaching of the doctrine of phagocytosis would thus appear, as Mr. Kanthack pointed out, to resolve itself into this, that what we formerly in our ignorance referred to the organism as a whole, we now refer to the individual cells of that organism. I have already replied to this objection, so far as it applies to the cells of the body as a whole; I have now to submit that in going further, and referring to certain particular cells of leucocyte and lymphoid nature, a special *rôle* in combating infectious disease and in conferring immunity, the doctrine of phagocytosis is not only an advance, but constitutes, in my opinion, a great advance in our knowledge of the mechanism and nature of immunity.

I base this belief on grounds independent altogether of bacteriological studies; on data, namely, derived from my study of the physiology and pathology of the blood, and I will now endeavour to make these grounds clear.

The changes relied on by the opponents of the phagocytic doctrine of immunity affect in a special degree, if, indeed, not exclusively, the plasma and serum of the blood, and are to be referred to antecedent changes in the cells of the body as a whole, rather than in any particular group of cells.

In this view I recognise a great resemblance to one still widely held by both physiologists and pathologists regarding the constitution of the blood and blood-plasma, namely, that the composition of the blood at any time is determined by the united action of all the tissues of the body.

As I had occasion to point out in the Arris and Gale Lectures of 1889, such a view is not supported by facts. The facts, on the contrary, point to a certain class of cells grouped for the most part in relation to a particular portion of the circulation as being primarily, if not exclusively, concerned with the constitution of the

blood-plasma, whether in building it up or in effecting alterations in it.

These cells are the leucocytes of the blood and the mass of lymphocytes lying in relation to the portal tract, especially those of spleen and alimentary tract.

It is a coincidence, to which I am inclined to attach not a little importance, that the class of cells thus found to be mainly responsible for the constitution of the plasma is precisely the same group of cells found by the upholders of the doctrine of phagocytosis to possess phagocytic properties in a specially marked degree; and that the chief seats of phagocytic action outside the circulation itself are, as is agreed to by all, in the first place the spleen, and, as has been clearly shown by Ruffer, the alimentary tract.

Action of Spleen in Relation to the Blood and to Infectious Diseases.—It is not my intention to adduce here or now the evidence on which the above conclusion is based, so far, at least, as the leucocytes generally and the lymphoid cells of the gastro-intestinal tract are concerned. Suffice to say that I have always found changes in the constitution of the plasma associated with evidences of great activity on the part of these cells—nuclear division, increased fragmentation, and formation of granular *débris*. and as to the important part taken by these cells as phagocytes, I leave to others who follow afterwards in this discussion to speak. In the hands of Dr. Ruffer and others I have no doubt ample justice will be done to that *rôle*.

For myself I propose to confine my attention solely to the spleen, and endeavour to establish the justice of the claim made on its behalf by the doctrine of phagocytosis, that its cells have a special phagocytic function independent altogether of the scavenging function common to them and other active cells. In particular I hope to show that they have what is claimed for them, and to a less degree for the leucocytes, by the phagocyte doctrine a greater selective power than other cells of the body, and that this selective power is specially exercised by them in relation to causes tending to affect the constitution of the blood-plasma.

The observations I am now about to refer to were not made with any reference to their bearing on the doctrine of phagocytosis, a circumstance that should, in my opinion, enhance any value that may attach to them in this relation.

The evidence I would adduce from them relates to the action of

poisons on the blood (1) in the presence, and (2) in the absence of the spleen. Briefly stated, it goes to show that the power possessed by certain drugs of altering the constitution of the blood depends primarily on the action of the splenic cells, and not on the cells of the body generally.

My experiments show for the poison toluylendiamin that its well-known destructive action on the blood is in an altogether special degree dependent upon the presence of the spleen, and that in the absence of that organ animals (rabbits) can tolerate about twice the dose without the slightest effect that would otherwise suffice to produce recognisable changes in the blood.

This difference in the action of poisons on the blood when the spleen is present and when it is absent does not apply to substances whose action on the blood is mainly physical, such as distilled water or glycerine, or, although to slightly less degree, pyrogallic acid. Nor is the power thus possessed by the spleen in the case of certain poisons due to any scavenging function on its part, and to the presence of a greater quantity proportionately of the substance in the spleen than elsewhere. On the contrary, by a method that enabled me to recognise the presence of even one hundredth part of a milligramme of the above poison, and whose margin of fallacy I found to be by accurate control less than $\frac{1}{2}$ per cent., I was able to show that the amount present in the spleen was less than in any organ of the body and less than that in the blood.

The result I interpret as showing that its injurious action on the blood was not a direct one, but an indirect one due to the intermediate action of certain cells, notably those of the spleen.

The bearing which these observations have on the subject now under discussion, the *rôle*, namely, of the cells of the spleen in modifying the constitution of the plasma of the blood, will, I trust, be obvious. For the subject of immunity and of phagocytosis in relation to immunity involves a consideration not only of the action of cells on microbes, but also of the action of cells on the products of these microbes. And these experiments appear to me clearly to establish that as regards these products, whose action can in no case be considered a purely physical one, their action on the plasma of the blood, for good or for ill, must in a very special degree be dependent on the action of the splenic cells —of cells, that is, that are claimed by the doctrine of phagocytosis to possess this phagocytic power in a special degree. *They clearly*

show at least for the products, what that doctrine claims to be also the case for the microbes themselves, that the splenic cells possess a special selective power that must render their action of the very greatest importance in the struggle against infectious disease. And we are not without more direct evidence that such is the case. A series of experiments have recently (1889) been published by Bardach, showing that the absence of the spleen affects materially the chances of recovery from infectious disease. His experiments were made on dogs, which are not naturally susceptible to anthrax even when inoculated subcutaneously; when it is injected into the blood they also resist, although a certain number succumb. After removal of the spleen they become much more susceptible. Thus out of twenty-five dogs whose spleens were removed, no fewer than nineteen died, while out of the same number of normal dogs similarly inoculated with anthrax only five died.

On the humoral theory of the nature of immunity it is difficult to understand how the absence of the small quantity of serum—to whose antitoxic and antibiotic properties recovery in such cases is ascribed—presumably present in the spleen could make a difference of such vital importance. Moreover it is not easy to reconcile these facts with Dr. Klein's contention, that even when phagocytes are present it is as probable that the microbes find themselves as comfortable within the cells as outside them. If such were the case, the spleen ought really to be a favorable seat for the growth and multiplication of bacilli rather than the converse; and its removal should rather increase than diminish the animal's chances of recovery.

It must not be supposed for a moment as tending to weaken the force of this argument that the animal, after the removal of its spleen, is in an unhealthy state. On the contrary, except in respect of its power of resistance to the action of poisons and microbes, it appears to be in no way affected by the operation, as I have constantly had occasion in the course of my experiments to observe.

Conclusions.

In conclusion, I would formulate in a few words the chief grounds on which I think the doctrine of phagocytosis appears to have advantages over the one which has been opposed to it. I am disposed to claim for it that in revealing to us, as it has done for

the first time, the potentiality possessed by cells of directly combating the attacks of virulent microbes, it has added much that is not only new, but is also valuable and important regarding the means by which infectious disease is combated, and that our knowledge of the bactericidal properties of blood-serum, to which so much importance is attached by the opponents of the phagocyte doctrine, is itself the direct outcome of the attention drawn by Metschnikoff to the action of cells.

So far from being antagonistic, the two doctrines—the phagocytic and the humoral—mutually supplement and support each other; disproof of the phagocytic theory, so far from proving the correctness of the humoral, tends, in my opinion, to weaken it. Both theories recognise the existence of antitoxic and antibiotic substances in blood-serum and blood-plasma; but it is, in my opinion, the peculiar merit of the phagocytic as opposed to the humoral doctrine that it subordinates them in interest and importance to action of the cells from which they admittedly derive their origin. If a choice has to be made between the two views, the one we can least do without is that which attaches a preponderating importance to the cells of the body rather than to the fluids, to the action of the cells rather than to the products of that action, to the agents rather than to the instruments.

I am disposed to claim for the phagocyte theory that, while it does not profess, as its opponents allege, to be in any way a complete or satisfactory explanation of the phenomena of immunity as a working hypothesis—and it is that we must first look for—it is in all respects more logical, more tenable, more in consonance with the teachings of cellular pathology, and I would almost say more biological than that which ascribes to the fluids of the body the first *rôle* in protecting it against infectious disease.

On both views the final nature of the change, whether in cell or in product, is unknown; but as the change in the cell must necessarily precede that in the product, and the doctrine of phagocytosis directs most attention to the cells, that doctrine has, in my opinion, claims on our support out of proportion greater than any teaching that would even temporarily draw our attention away from the cell to the fluid in which it lies, that would exalt the product at the expense of the producer.

Lastly, I claim for the phagocyte doctrine that in attaching special importance to the action of certain cells—leucocytes of

blood, cells of spleen, and lymphocytes generally—it draws attention to facts of wide physiological importance, namely, *that it is precisely these cells that govern, in a special degree, the constitution of the plasma and blood-serum.* Whether acquired immunity be due to a direct phagocytic action of these cells, or to antibiotic or antitoxic properties of the plasma of the blood, it is this particular group of cells that must have been specially affected by the changes left on the body by the preceding attack.

Dr. SIDNEY MARTIN said that the question might be studied in two directions: (1) as to what rendered an animal naturally immune to a disease, and (2) as to mode of production of experimental immunity. Immunity produced by experiment was a much better method of research than the investigation of natural immunity, inasmuch as the conditions of experiment were controllable.

Of the several examples of experimental immunity now known, that of anthrax was perhaps the best to be discussed, as the morphology of the bacillus anthracis was so well known.

In the classical experiments of Pasteur the attenuated bacillus anthracis when inoculated into a sheep was found to produce some degree of illness, which passed off. The animal was rendered immune, as the inoculation of a virulent bacillus one month after vaccination failed to produce death. What they wished to know was what happened to the virulent bacilli injected; why did they not kill the sheep as they did in an unprotected animal? Those who depended on phagocytosis for an explanation would say that the action depended on the activity of the leucocytes at the seat of inoculation of the virulent bacilli, and that these leucocytes effected the destruction of the bacilli. This explanation was, to his mind, by no means sufficient. They had in the experiment just quoted first the injection of an attenuated living virus, and then a subsequent inoculation with a virulent virus, also living. Now, as he had shown in his last paper in the Report of the Medical Officer of the Local Government Board (1890–91), the attenuated anthrax bacilli formed the same chemical products as the virulent bacilli; but whereas the attenuated bacilli would grow well for a time in a culture medium (such as alkali-albumen broth) in which they could form their products, after a certain period they stopped growing; the virulent

bacilli would, in a similar solution, go on growing for a much longer time, and would produce a much larger quantity of chemical products than the attenuated. A bacillus, whether attenuated or virulent, acted by means of its chemical products. In the case, therefore, of Pasteur's sheep experiment it must be said that immunity was produced by means of the chemical products of the attenuated bacilli, and yet the virulent bacillus which produced the same products did not kill the animal. Its natural growth and activity had been inhibited. How could this be explained? Part of the explanation appeared to be that the inoculation of the attenuated virus accustomed the animal to the specific chemical poison of the bacillus. Several instances of tolerance of drugs, such as morphine and arsenic, were well known in pharmacology—a tolerance which, when established, would enable the person to take with impunity a dose of the drug which would be fatal to an unprotected person in a few hours.

A certain degree of tolerance to virulent anthrax bacilli might be established in animals by means of the chemical products of the micro-organism, as in the following experiments quoted:

A guinea-pig was inoculated under the skin of the right thigh with 10 milligrammes of the anthrax albumose and 9 milligrammes of the alkaloid; under the skin of the left thigh, with a "mash" of the spleen of an animal which died of virulent anthrax. This dose of the chemical products produces only a slight physiological effect in guinea-pigs. The animal lived four days and a half, whereas the control animal died within twenty-four hours. The lesions found were those of anthrax. In a second guinea-pig, done at the same time, the same dose of chemical products and of "splenic mash" were mixed together and injected under the skin of one thigh. This animal showed no change for twenty days, when it died somewhat suddenly. A *post-mortem* examination showed no œdema at the site of inoculation, and only a slight enlargement of the spleen, which was very pale.

In the first experiment he should say that part of the explanation of the delay of death was that the chemical poisons influenced the organs (of the central nervous system) which they selected for their action, and that the effect of this action was to prepare them for the onset of the larger amount of products produced by the virulent bacillus, but that the alteration in the tissues was too slight to prevent death. Such an experiment was a very imperfect

imitation of what occurred after the inoculation of an attenuated living virus, for the products of the attenuated bacillus, being gradually formed, were gradually absorbed, so that the physiological effect was one of repeated small doses of the specific poison, the action lasting for a long period of time. That the chemical products of pathogenic bacteria were a long time in the body he knew from his own experiments. A single dose of the anthrax albumose would produce fever lasting five days, and with the products from other diseases he had found evidence of their presence in the blood ten or even twenty-four days after inoculation. It was probable, therefore, that the chemical products of attenuated bacilli would remain longer in the body than when the chemical products were simply injected, and he had but little doubt that this retention of specific chemical substances in the blood (which they profoundly affected) had an important bearing on immunity.

Why, it might, however, be asked, did not the virulent bacillus grow in the artificially immune animal? Even supposing the chemical products of the attenuated virus were present in the body at the time of inoculation with the virulent bacilli, could they be supposed to stop the growth of the bacilli, or weaken them so that they behaved like the attenuated virus in having a short existence? The second experiment appeared to bear on this point, for mixing the chemical products with the bacilli delayed death for twenty days, while in the first experiment, where the injection occurred once on each side of the body, death was delayed for only four days and a half. Now, if virulent bacilli were grown in a flask containing a nutrient medium from which they could form their products, after a time the growth stopped, just like peptic digestion, where the products choke the action of the ferment. It was hardly possible, he thought, that the small amount of products which might be present in the body after the injection of the attenuated virus could choke the growth of the virulent bacillus by their own action, but it was not improbable that the profound effect which they had on the blood might diminish the advantages which that liquid possesses of serving as a nutrient medium for the bacillus. He did not pretend that what he had stated explained immunity, but they were matters for thought and for future experimentation, as showing that there was something beyond phagocytosis in the question of immunity.

Dr. A. E. WRIGHT said he did not intend to enter upon the main issues of the debate, as he had no original observations to communicate which had a direct bearing upon phagocytosis as a method of resisting disease. Without, however, taking a side as a "phagocytist" or a "humoralist," he might perhaps be permitted to bring into hotchpot a few observations upon the subject of chemical immunity, which might turn out to be pertinent to the matter in discussion.

The history of the subject he had been engaged upon was shortly as follows:—The late Dr. Wooldridge, in 1888, described a method of what he termed "chemical protection" against anthrax. He found that when he administered tissue-fibrinogen to rabbits they remained immune against a subsequent injection of anthrax. He employed tissue-fibrinogen solutions, which were prepared either from the thymus or from testicles, and which he subsequently boiled in order to render them sterile. His results did not appear to have been uniformly successful, and he seemed to have attributed the failures in great part to the fact of his protective fluid becoming inert during the process of boiling. Dr. Wooldridge died, and his work was left in this incomplete condition.

Mr. Hankin, of Cambridge, in whose mind a somewhat similar idea with regard to chemical protection had been simmering before the date of Wooldridge's publication, was the next to take up the matter. He adopted the term "defensive proteids" for the albuminous substances in which protective chemical properties were supposed to be resident, and he proceeded to graft the idea of a bactericidal power on to the more generic conception of a defensive proteid. He suggested, for instance, that if Wooldridge's tissue-fibrinogen really conferred an immunity against anthrax, it probably conferred that immunity by virtue of a bactericidal property with which it was endowed. Dr. Wright gathered that Mr. Hankin had since abandoned this suggestion.

The next observation of Mr. Hankin which he wished to bring into relation with Wooldridge's work was his observation that a particular substance—or more probably mixture of substances—of protective virtue could be extracted from the spleen of the white rat—that is, from the spleen of an animal which was known to be relatively immune against anthrax. This substance, or mixture

of substances, under the name of an alexin, was, if he understood Mr. Hankin aright, to be considered responsible for the measure of immunity which the white rat possessed over the more susceptible brown rat. He would endeavour to deal very briefly with the work of those two observers.

With regard to Wooldridge's work, it was obviously necessary to reopen the investigation of the subject by repeating his experiment, and then to proceed to isolate the constituent to which the immunity was due. It also seemed desirable to adopt some more appropriate method of sterilisation than that of boiling, for Wooldridge himself had recognised the disadvantages which were associated with this method.

Dr. Wright had given an account of his attempts to do these three things in a paper[1] which was read at the International Congress for Hygiene last year. He there showed that sterilisation by means of a Chamberland's filter might with advantage be substituted for the method of heat sterilisation. He further showed that tissue-fibrinogen was a proteid substance which belonged to the class of the nucleo-albumens or nucleo-proteins. Lastly, he reported several series of experiments in which he succeeded, by means of tissue-fibrinogen injections, in prolonging or preserving life in rabbits which had been inoculated with virulent anthrax.

Certain defects in his experiments, in the matter of preserving his tissue-fibrinogen solutions in an absolutely aseptic condition throughout the experiments, he had since remedied, and had obtained exactly the same results with absolutely sterile solutions. The results of his experiments on anthrax were, that he had never made a series of experiments without obtaining either a prolongation of life, or a complete cure, by means of the tissue-fibrinogen injections. The results were, however, as yet by no means satisfactory, and there were difficulties to be contended with in the matter of the attenuation of the tissue-fibrinogen solution during sterilisation by the retention of a portion of the tissue-fibrinogen in the pores of the filter.

Having got thus far, he was naturally anxious to obtain some information as to the manner in which this curative property of tissue-fibrinogen became effective. He found, in conformity with Wooldridge's previous observations, that anthrax could be got to grow in

[1] 'Brit. Med. Journ.,' Sept. 19th, 1891, p. 641.

tissue-fibrinogen solutions. He therefore concluded that whatever the effect of tissue-fibrinogen might be due to, it was clearly not due to a bactericidal power. Mr. Hankin, he believed, agreed with him in this.

Dr. Ruffer had suggested to him at the outset of his work that tissue-fibrinogen might possibly act as a cell stimulant. From this, and from a paper of Groth[1] upon the effects of an intravascular injection of leucocytes, he had turned his attention to the examination of the blood, and to the enumeration of the leucocytes after tissue-fibrinogen injections. These enumerations gave at once some very tangible results. In every case the injection of tissue-fibrinogen was observed to be followed by a remarkable increase in the number of leucocytes. He had repeatedly seen them increased to as much as six times their normal number, and at the same time a remarkable poikilo-leucocytosis appeared, some of the corpuscles being of enormous size, and others again of very diminutive size. At this stage of the investigation he came across the very remarkable paper of Horbaczewski's[2] upon the physiological effects of nuclein.

Now, since he had shown in his previous paper that nuclein was a constituent of tissue-fibrinogen, and since Horbaczewski proved that the administration of this nuclein resulted in the production of a leucocytosis, he naturally turned to investigate whether the protective effects of a tissue-fibrinogen solution could be obtained by an administration of its nuclein moiety alone. He anticipated that he should incidentally reap the advantage of an exact dosage, and also an advantage in the matter of obtaining aseptic solutions with greater facility. He had only just begun the investigation of the matter, but had already been able to satisfy himself that a very remarkable prolongation of life resulted from the administration of the nuclein before an anthrax inoculation, and that this prolongation of life was associated with an increased leucocytosis.

In what relation did this chemical protection stand to Mr. Hankin's researches on immunity? Mr. Hankin obtained his alexin from the spleen of the relatively immune white rat. He obtained it by extracting it with what was practically a normal saline solution. If there were any tissue-fibrinogen present in an organ a watery solution would extract it, and in the spleen, where

[1] 'Dissert.,' Dorpat, 1884.

[2] 'Sitzber. d. Wiener Akad.,' C. Abth., April, 1891.

there were leucocytes in relatively large quantities, the main constituent of leucocytes, that was tissue- or cell-fibrinogen, must of necessity be present. Therefore Mr. Hankin's extracts of white rat spleens would contain tissue-fibrinogen. Mr. Hankin's next proceeding was to precipitate his watery splenic extract with alcohol, to redissolve the resulting precipitate in water, and to employ this last extract, after dialysing away the salts, as a protective fluid. The method of preparation was an almost ideal method for ensuring the presence of tissue-fibrinogen in Mr. Hankin's final solution, for while the alcohol precipitation might exclude other elements which might be present in the splenic extract, it certainly could not exclude the tissue fibrinogen, for this substance was not rendered insoluble by alcohol.

He thought, therefore, that Mr. Hankin's alexin was the same thing as Wooldridge's tissue-fibrinogen, or at any rate that it could not fail to contain it. In this connection he would point out that the nuclein with which Horbaczewski's experiments were conducted was prepared from the leucocytes of the spleen. With regard, lastly, to Mr. Hankin's observation that his alexin was found only in the spleen of the relatively immune white rat, he suggested that this might possibly depend upon a greater development of the adenoid tissue of the spleen in the white rat, for it was well known that the spleen played an important part in the conflict of the organism with the micro-organisms of disease. A greater development of adenoid tissue would go hand in hand with a larger percentage of tissue fibrinogen in the extracts.

In conclusion he adverted for a moment to the newer development of the Metschnikovian doctrine, which aimed at the reconcilement of the opposing schools of phagocytists and humoralists, by assuming that the disintegration products of the white corpuscles played a part in the conflict of the organism with infective disease. Each of these chemical disintegration products might possibly act in a protective manner by virtue of either a chemiotactic power, a bactericidal power, or a cell-stimulating power.

Dr. Ruffer had determined for him that tissue-fibrinogen solutions had a powerful positive chemiotactic power. The observation seemed to him of interest, as it might help to explain how fresh leucocytes might be attracted to the seat of infection after the bacteria had got the better of the first leucocytes which had arrived on the scene.

With regard to the bactericidal power of tissue fibrinogen, it seemed to him that the question had not finally been decided in the negative, as his cultivation of anthrax in tissue-fibrinogen solutions were made in tissue-fibrinogen derived from the testicle, and there might conceivably be points of difference between the two varieties of tissue-fibrinogen. On the other hand, he thought that great caution was required in drawing inferences from a bactericidal property of a solution in a test-tube as to the bactericidal power of the same substance in the organism, because such a substance as tissue-fibrinogen was rapidly broken down inside the organism.

With regard to the cell-stimulating powers of the products of the decomposition of leucocytes, it had already been seen that tissue-fibrinogen possessed such stimulating properties in a high degree. He thought that tissue-fibrinogen and nuclein might be regarded as cell manures; for by whatever method these substances were introduced into the organism, they were invariably found to produce a leucocytosis.

Mr. J. G. Adami.—When the time allowed to each participant in this evening's discussion is necessarily so short, perhaps the best method of attacking this subject of immunity is to start with the best and most complete series of observations in the case of one disease, observations that are both recent and reliable, and then, accepting the facts so gained, to observe how they oppose or confirm the various theories which have been brought forward. For this purpose I would select the very full and pregnant research of Klemperer and Klemperer upon pneumonia. The results of these observers may briefly be stated as follows:

i. Immunity against pneumonia can be bestowed upon susceptible animals by introducing into the tissues the sterilised products of growth of the pneumococcus. This immunity is in general but of a temporary nature.

ii. Such immunity induced by injections of bacterial products does not immediately manifest itself; indeed, fourteen days must elapse before the simple products bring about their effects. But if the sterilised products be heated either to from 106° to 107·5° (Fahr.) (40—41° C.) for three to four days, or to 140° (60° C.) for two hours, then injections induce immunity within four days.

iii. The warmed "vaccine" leads to a reaction of but short

duration; the unwarmed brings about a long-continued febrile state, at the end of which the animal becomes immune.

iv. Thus the fever with its elevation of temperature and the antecedent heating of the vaccinal material induce the same result; one or other process would seem to be necessary in order that sterilised bacterial products develop immunity.

v. But, further, the blood-serum of a "protected" animal injected into the veins of a susceptible animal confers immediate immunity. There is no delay. Evidently, therefore, some substance is present in the blood-serum of an animal made immune, a substance not present in the sterilised culture fluids of the pneumococcus. The bacterial products, therefore, do not *per se* bring about immunity, but through the febrile reaction some other body having immunity-conferring properties is gradually developed.

vi. What is more, this same substance has curative properties acting not so much on the pneumococci themselves (for in its presence these continue to proliferate), but upon the poisons or toxines manufactured by them.

vii. Hence Klemperer and Klemperer distinguish two *proteids;* the *pneumotoxine,* which can be isolated from cultures of the pneumococcus, and the *antipneumotoxine* to be obtained from the serum of immunised animals.

It is unnecessary for me to dilate upon the way in which this work of the two Klemperers fulfils and elucidates the previous observations of Salmon and Smith, Christmas, Roux and Chamberland, Hankin, Bouchard and his school, Brieger and Fraenkel, &c., upon bacterial products, of Wooldridge, Christmas, Hankin, Buchner, Hankin and Martin, Tizzoni and Cattani, and Fraenkel upon proteid bodies capable of inducing immunity, and (in the case of some of these observers) upon the antitoxic properties, as opposed to the bactericidal properties of such proteids. Nor need I do more than point out the light that these observations throw upon the meaning of the febrile state. Evidently, as shown by a large number of recent studies, the phenomena of infection and immunity are at base chemical; certain substances are produced by the bacteria on the one hand, by the organism on the other, whose action is of a chemical or chemico-physical nature.

But now comes the question, how is this action exerted within the body? Are bactericidal and antitoxic substances normally free in the blood, are they developed within special cells, or

are they generally distributed throughout the tissues of the body?

In the first place, it cannot be too strongly insisted that their presence in blood-serum is no certain indication of their presence in blood-plasma. Blood-serum and blood-plasma exhibit marked difference in their characters, and nothing is more marked than this difference in the bactericidal powers of the two fluids. An animal which is most susceptible to a given disease has time after time been shown to yield a serum capable of destroying large numbers of the micro-organisms causing that disease, and at the risk of repeating what is well known to many I would again call attention to Lubarsch's classical observation that, whereas 10,000 to 12,000 anthrax bacilli are all that can be injected into the circulation of a rabbit without causing a fatal disease, 1 cubic centimetre (15 minims) of a blood-serum of such a rabbit will in a few minutes destroy the same or a much greater number of the bacilli. While I am far from convinced that under no conditions can the plasma become bactericidal or antitoxic, I still think that sufficient satisfactory evidence has not yet been brought forward in support of the humoral theory. The cases mentioned by Prof. Klein are not without flaw—the rapid diminution of the number of bacteria present in arterial or venous blood is not conclusive evidence that these bacteria have undergone destruction in the blood-plasma (phagocytosis being as yet undeveloped). Prof. Klein and the humoralists have to bring forward surer proof than has yet been adduced that the bacteria, as foreign bodies, have not been arrested in the capillaries of various organs, and that the diminution of their number in the circulating blood is not caused by such a filtration process.

Again, while I am prepared to admit freely that bactericidal and antitoxic substances may appear or be developed in the cells forming many of the tissues of the body, I hold that it has yet to be proved that this can obtain to any great extent. We are still without proof that, save in the case of organs formed largely of leucocytes and potential phagocytes, the tissue can have powers at all comparable to those possessed by the serum and body fluids.

We are, therefore, driven to the third possibility, namely, that the difference between serum and plasma depends upon an alteration in the condition of the white corpuscles, and that the leucocytes are a most essential factor in the production of immunity.

There is not time here to bring forward all the arguments in favour of this view, but this I may say: what other interpretation is to be placed upon (not simply the engorgement, but) the enlargement of lymphatic glands, the enormous increase in the number of white corpuscles in the blood in zymotic disease (under conditions to be referred to later), the determination of leucocytes towards regions of bacterial invasion, unless it be that the leucocyte plays a most important *rôle* in protecting the organism? It is true there are conditions in which it is wanting. In pneumonia, for example, Tchistovitch has shown that where the virus is not very powerful, there an increase occurs; where the virus is very strong, there a diminution is to be made out in the leucocytes of the blood. The same occurs in regard to the amount of diapedesis resulting after local invasion, this depending upon the virulence of the invading organism. Taking into consideration general rather than local infections, we learn that the leucocytosis is dependent upon the reaction of the organism to the soluble products of the virus.

That the leucocytes can possess bacteria-killing powers is supported by Hankin's observations upon the lymphatic glands and spleens of refractory animals, in which he showed that from these organs, composed as they are largely of mature and immature leucocytes and the parent cells of the same, can be obtained a bactericidal substance acting specifically upon the microbes to which the animal was refractory. It is impossible for me to criticise Dr. Woodhead's objection to this, namely, that Dr. Wright has grown micro-organisms freely upon leucocytes, until the conditions of these experiments have been fully described.[1]

To come now to the assumption of bactericidal powers by blood-serum, I would remark that, as Rauschenbach has shown, and as a matter of common experience, coagulation of the blood and production of serum is accompanied by a great disintegration of certain of the white corpuscles,[2] and I would suggest that to this disintegration is due the presence of bactericidal substances in the serum. Just as from fresh blood and intact white corpuscles no fibrin ferment is obtainable, so it may be that the intact leucocytes do not *normally* contain bactericidal substances, but precursors

[1] In a verbal communication after the discussion Dr. Wright stated that Dr. Woodhead erred in ascribing these experiments to him.

[2] Upon these points see the fuller details given by Dr. Wright in the 'Lancet' of February 27th, 1892.

thereof. Possibly this is fitted to explain Dr. Woodhead's contention with reference to quinine.

I am unwilling that this working hypothesis, whereby I have attempted to reconcile for the time being the divergent results of a host of capable workers, should be dubbed a theory; still more do I regret that it should have been accredited to me. For, while I have worked it out along my own lines, its origin is to be found in Mr. Hankin's work, and to all intents and purposes this is the hypothesis brought forward by Hankin at the International Congress last year. If for no other reason, I am glad to join in this evening's discussion in order that honour may be given where honour is due.

Lastly, as to the way in which the leucocytes act upon the bacteria, I cannot help being impressed by the fact that the more perfect the methods employed the greater is the phagocytosis observable in the course of resolution of disease, and I must conclude that even though leucocytes have other methods of acting upon bacteria and their products, phagocytosis is a most important, probably the most important, factor in the production of immunity. Professor Burdon Sanderson's main objection, that leucocytes are to all intents and purposes independent organisms, and that therefore they cannot reasonably be expected to act in accordance with the needs of the organism, is, it seems to me, based on the idea that leucocytes are generation after generation propagated in the blood, free from the fixed cells of the body. But this is scarcely the accepted view. Very little mitosis of the leucocytes occurs in the blood, whereas the characteristic mitotic areas in the lymph-glands offer an almost certain indication that the proliferation of leucocytes occurs in regions where the parent cells may be regarded as fixed and capable of being influenced by nervous and other stimuli. It is to these parent cells rather than to the free, motile leucocytes, with their short span of life, that we must look to explain continued powers of resistance to bacterial products on the part of leucocytes, the development of increased resistance, the development of immunity.

Mr. T. J. Bokenham.—I have worked especially with erysipelas, and it seems to me that this disease offers some phenomena which must be explained before the question of the causation of immunity can be definitely settled.

A. *Different effects of injecting cultures of true* Str. erysipelatis *into rabbits and guinea-pigs.*—Inoculation of a virulent culture into the ear of a rabbit will produce a typical spreading erysipelas. Pus formation very seldom takes place, but without doubt the lymph, which is present in great abundance, is very rich in leucocytes, and contains also streptococci while the process is advancing, but none during the period of defervescence. This is proved both by the results of microscopical examination and of inoculation.

If a guinea-pig and a rabbit be inoculated from the still virulent exudation, the latter will contract a disease in every respect similar to the first, while the guinea-pig will show no phenomena either local or general. Here there is no crowding of leucocytes to the point of inoculation, but still I have not found that a guinea-pig is susceptible to erysipelas such as is virulent for rabbits. I think I may be able in the future to offer an explanation of the divergence of this statement from those made by some others, but this is not the time at which to do so. However, it would seem that unsuitability of soil rather than active phagocytosis played the active part in this case of apparently "natural" immunity.

B. Another class of observations also requires explanation—*the alteration in virulence of the* Str. erysipelatis *under varying conditions.*

(1) A culture of *Str. erysipelatis* which has become too attenuated to produce the characteristic lesion in a normal rabbit, may, in a rabbit prepared by the simultaneous intra-peritoneal injection of a sterilised culture of the *B. prodigiosus*, be made to produce the typical signs of erysipelas at the seat of inoculation. In other words, a rabbit which is immune to a streptococcus of a given low virulence can be made susceptible by preparation in this way; and, further, in this process the virulence of the erysipelas is definitely increased, for inoculation from this rabbit to a normal one will give rise to a typical erysipelas in it. On passing the erysipelas through one or two more rabbits, along with the products of *B. prodigiosus*, the character of the resulting disease becomes changed, so that at last, instead of a local disease, I have been able to produce a general infection without signs of local reaction at the point of inoculation. The blood then becomes highly infective, and contains streptococci, which produce typical erysipelas in normal rabbits.

Undoubtedly here the local cellular infiltration seems to have played a part in the localisation of the disease, and the presence of

the products of the *B. prodigiosus* appears to me to have hindered the leucocytes from performing their natural protective function.

(2) A similar observation on the difference between the course of erysipelas in a normal rabbit and in one vaccinated against the blue pus bacillus requires explanation. I have found that a rabbit vaccinated against the *B. pyocyaneus*, and subsequently inoculated with the *Str. erysipelatis*, develops, not a local lesion, but a general fatal infection, the blood becoming infective, as in the case of animals prepared with sterile cultures of the *B. prodigiosus*. In another normal rabbit, however, this blood causes, not a general, but again a local disease. This observation seems to me to indicate that in an animal vaccinated with the products of the *Bacillus pyocyaneus* the leucocytes are in some way prevented from travelling towards the erysipelatous centre, where they are needed in order to prevent a general infection; and this view receives some confirmation when compared with the observation of Charrin and Gamatéia ('Comptes Rendus de l'Acad. des Sciences,' June 2, 1890), that if croton oil be applied to the ear of a rabbit saturated with the products of the *Bacillus pyocyaneus*, no inflammatory reaction takes place at the point of application, as happens in the case of a normal rabbit.

Of course this view requires much further experiment before it can be proved, and I only throw it out tentatively.

Association of attenuated erysipelas with a common mould seems also to increase both the virulence of the streptococcus and the local reaction, for I have found that a culture which, from age, was incapable of producing any local symptoms in a rabbit, after contamination with *Penicillium glaucum*, gave rise on inoculation to an acute local erysipelas with pus-formation. It seems to be definitely shown here that the mixed infection gave rise both to increased leucocytosis and increased virulence of the *Str. erysipelatis*. Certainly the penicillium by itself gives rise to no such reaction; neither did the culture of the streptococcus before contamination. I should state that in the process of local reaction the mould became entirely destroyed, cultures made from the exudation giving, during the advance of the disease, the *Str. erysipelatis* in a state of purity, and during the defervescence giving no result. This observation is, without doubt, difficult of interpretation, and I am not aware that any parallel instance is recorded in bacteriological literature in which a non-pathogenic mould, when associated with a microbe which is no longer capable of exciting a local

reactive inflammation, gives rise at once to an intense local reaction accompanied by a restoration of the lost virulence of the pathogenic streptococcus.

Dr. Armand Ruffer.—When beginning their remarks on immunity and phagocytosis Professor Burdon Sanderson and Dr. E. Klein stated that they could not accept Professor Metschnikoff's views. I will imitate their candour, and define my position in the same manner, by stating at once that I accept Metschnikoff's theory in its entirety.

Not one of the speakers has explained what he means by immunity; and surely this is the first point to decide. Immunity from a given disease means freedom and exemption from that disease. As far as I am aware, there is no animal, whether naturally resistant or protected by artificial means, which cannot be killed by the introduction of a specific microbe, provided a sufficiently large dose be used. To talk of an animal being immune against a given microbe is to speak of something which does not exist; and although I must confess to having used the word myself, I would in future rather talk of animals naturally resistant and artificially protected.

Now when a naturally resistant or artificially protected animal is inoculated with a virus, I believe that the destruction of the micro-organisms in that animal is accomplished by the amœboid cells, which, for the sake of convenience, we will call phagocytes. I am not aware that Metschnikoff, or any of his pupils, ever said that this was the only cause of the increased resistance of such animals. Metschnikoff certainly never said so, but in his writings and in conversation he has simply stated—and indeed proved—that the process of phagocytosis was *one* of the most important factors in the acquired, or natural, resistance of a given animal against a given micro-organism.

Dr. Woodhead has already stated what we know of the origin of phagocytes, and I would not enter into the discussion of this question were it not that I must make a personal explanation. I have not said anywhere that *all* microphages, epithelioid cells, &c., were derived from leucocytes. What I have said is, that in the cases I have observed the macrophages were derived from small lymphocytes. Were any proof necessary that such an origin of plasma, or epithelioid, cells is of no infrequent occurrence, I would point out that the development of these cells can be seen in the intestines

of various animals, where they wander into the epithelium layer; that they have been found in the blood-vessels; that when vermilion is injected into the veins of an animal, similar large cells seize on the powder circulating in the blood, and carry it into the neighbouring tissues—into the medulla of the spleen or alveoli of the lungs, for instance; that no such cells are present in the alveoli of the lungs of a newly born guinea-pig until they have been attracted there by some kind of noxa; and, lastly, that in Invertebrata the transformation of an amœboid cell into a fixed cell has actually been followed day by day in the living animal.

Let us, however, pass at once to what happens when wandering cells have taken bacilli into their interior; for there can be no doubt that leucocytes have that power, and that the organisms contained in cells undergo some kind of destruction. That is a matter of observation which everyone can notice for himself who possesses a good lens, a drop of frog's lymph, and a few anthrax bacilli.

In the first place, see what happens when a protected or non-protected animal recovers from an infectious disease, or even when it dies after having resisted the malady for a considerable time. In all cases which have been studied up to the present, phagocytosis is a well-marked phenomenon. Slight, or even absent, when the animal has no powers of resistance against a given microbe, it increases with a more resistant animal, or when an animal has been artificially protected, and reaches its maximum when the disease is essentially chronic, as in leprosy and tuberculosis. Lately I have been studying human pneumonia from this point of view, and I can safely say that the human lung in this disease exhibits, in their exquisite forms, all the phenomena of phagocytosis.

Dr. Klein, in his able criticism of Metschnikoff's theories, lays special stress on the fact that, in several instances, the process is reversed, and that the leucocytes are destroyed by the bacteria, and not the bacteria by the leucocytes. This he considers a fatal objection to Metschnikoff's theory. As far as I am concerned I may state that, in almost every one of my papers, I specially mentioned that a large number of amœboid cells perished in the fight. I have shown this to take place in the healthy rabbit's Peyer's patch, in the diphtheritic membrane, in actinomycosis, in tubercle, in *charbon symptomatique*, &c.

I will meet Dr. Klein on his own ground, and take as examples

two of the very diseases which he himself has mentioned as proving the fallacy of Metschnikoff's theory—namely, leprosy and tubercle. In many particulars these two diseases resemble each other strongly, for both are caused by a hard resistent micro-organism, and, pathologically, both are characterised by the fact that the micro-organisms, whenever present, set up intense inflammation.

Let us make a section through a leprous nodule, and stain it in the usual manner with logwood and carbol-fuchsine. I need not enter into the description of the epithelioid and giant cells always to be met with in leprosy, but at once examine the processes taking place in these cells. In some cases such cells, when crammed with bacilli, undoubtedly die, and this death is indicated by the degeneration of their nuclei, the vacuolisation of the protoplasm, and the apparent proliferation of the characteristic bacilli in the cells. That is one side of the picture, but let us look at the other side. In some of these cells the bacilli lose their definite outline and fuse together into a hard, solid, resistant mass, in which no structure is discernible even when use is made of the most delicate staining reagents and the highest powers at our command. In a later stage this hard resistant mass gradually breaks up and loses its power of retaining staining matter, until nothing is left in the cell but a clear space, which may be either a vacuole, or possibly a kind of membrane with which the bacilli have surrounded themselves. On one hand, therefore, we can follow the victory of the bacilli over the cells, and, on the other, we have that of the cells over the bacilli. True, in the large majority of cases of leprosy, the bacilli gain the victory, but are we not justified in thinking that the chronic character of the disease, which may last for months and years, is due to the way in which amœboid cells incorporate the bacilli and destroy a large number of them? Unfortunately the bacillus has means of defence of its own, and thus frustrates the beneficent endeavours of the cells.

It is an admitted fact that in cases of tuberculosis bacilli are often found in epithelioid and giant cells, and there is not the slightest doubt that these cells frequently succumb in the fight. Signs of degeneration are found in microphages, mono-nucleated, epithelioid, and giant cells, with a frequency which can leave no room for doubt. But what is not so easily observed is the other side of the fight, in which the bacilli perish. Metschnikoff has shown that signs of the encapsulation, decay, and death of the bacilli

are of the most frequent occurrence in the giant-cells of tubercle, and more especially in the giant-cells of those animals which exhibit a strong resistance towards the bacillus of tubercle. In man, indeed, such evidences of encapsulation are met with in the more chronic forms of tubercle, such as old scrofulous glands or calcified nodules in the lungs. In many cases of tubercle, therefore, the bacilli prove too strong for the amœboid cells; but that in many others the cells are victorious is proved by the frequency with which cured tuberculous lesions are found at the *post-mortem* examination of patients dying from some other disease. As Dr. Klein has said, in these diseases a great many of the leucocytes perish, but he might have added that the destruction of the bacilli is even more marked than that of the cells.

I am willing to allow the accuracy of Dr. Klein's experiment, when, on injecting a quarter or half a syringe of fluid containing anthrax spores or anthrax bacilli, he finds the anthrax bacilli in the blood a few minutes afterwards. Indeed, it would be wonderful were it not so, for the frog's phagocytes are able to arrest a certain number of bacilli, but not an immoderate number; they will arrest enough bacilli to kill a mouse, but not the number of micro-organisms which would kill an elephant. And similarly with vermilion. In my experiments I injected one drop of a saline solution holding vermilion in suspension, and found that it was absorbed through the agency of leucocytes. Had I injected a quarter or half a cubic centimetre, the vermilion might possibly have penetrated directly into the blood; but I hold that it is not a satisfactory experiment to inject into the lymph-cavity of a frog a large quantity of fluid, when the object in view is to study the absorption of solid particles.

In a former paper I have shown that in animals exhibiting some resistance against the bacillus of Chauveau, the disease was strictly limited to the point of inoculation and its immediate neighbourhood. When, however, from any cause, physical or chemical, the amœboid cells were prevented from approaching the virus, the disease became general and the animal died. Dr. J. H. Walker and myself have recently obtained one more confirmation of this law, as shown by the following experiments[1] with another micro-organism.

If an adult guinea-pig be inoculated subcutaneously with 0·25

[1] These experiments will be related in full at some future date.

cubic centimetre of a pure culture of the *Bacillus pyocaneus*, an abscess slowly forms at the point of inoculation. Twenty-four hours after the injection the point of inoculation is crowded with bacilli and well-filled phagocytes; but—and this is the important point—cultures made with the various internal organs prove absolutely sterile. The bacilli, therefore, are arrested at the point of inoculation by the amœboid cells, and this can be proved by microscopic examination.

Now if, at the same time that we inoculate the *Bacillus pyocaneus* on one side of the body, we inject on the other side a large dose of chloral hydrate, which is yet not sufficient to cause death, and repeat the dose from time to time, so as to keep the animal fully anæsthetised, it invariably dies within forty-eight hours, and all the organs contain the bacilli in incredible numbers.

It is easy to prove that in an anæsthetised animal the leucocytes are inactive. Let us take two small sponges, fill them with a pure culture of the *Bacillus pyocyaneu*, and place each under a guinea-pig's skin. One of these animals we leave as a control, whereas we inject the usual quantity of chloral hydrate under the skin of the other. Six hours afterwards, when we take out both sponges, we find the fluid in the sponge of the chloralised animal almost as clear as when it was introduced. A few leucocytes may be seen in it, ten or twenty at most in one cover-glass preparation, whilst the control sponge is filled with a thick purulent material, which on microscopic examination proves to consist of innumerable well-laden phagocytes. No wonder, then, that when the leucocytes refuse their work the bacilli should find their way into the tissues. We have vainly sought for any evidence to show that the fluids of chloralised guinea-pigs are better cultivating media for the *Bacillus pyocaneus* than those of a non-chloralised animal; in both chloralised and non-chloralised animals the bacilli seemed to thrive exceedingly well in the fluids of the living body. Here, then, we have another instance of the part taken by phagocytes in the limitation of the disease.

As to the substances which attract the amœboid cells towards the virus, they have been proved to be the poisons secreted by micro-organisms, or contained in their bodies. It is probable also that in some cases these poisons have the opposite effect, namely, that of repelling amœboid cells. I have lately gained considerable evidence to show that the same substance may attract or repel

leucocytes according to its state of concentration. I may mention one such experiment. If a small piece of sterilised sponge be soaked in pure turpentine and placed under a guinea-pig's skin, it will be found that, even after a lapse of twelve hours, not a single amœboid cell has penetrated into the sponge. Sections made through the sponge and surrounding parts show that the amœboid cells have emigrated in considerable numbers into the tissues around, but that they are arrested at a certain distance from the sponge, and can proceed no further. A piece of normal sponge placed a little distance off is absolutely crammed with amœboid cells, though the turpentine sponge contains none at all.

Now allow a similar sponge to soak in a very dilute solution of turpentine in olive oil, and place this sponge, together with another containing fine sterilised olive oil and a third soaked in pure turpentine, under the skin of a guinea-pig. After four hours the sponge with the solution of turpentine in olive oil is crammed with amœboid cells, whilst the other sponge soaked in olive oil contains but a few, and that in turpentine none at all. Here, then, we have the same substance exhibiting totally different effects according to the concentration with which it is applied. It is very probable that such is the case with bacterial poisons also, and there are already some experiments which support this view. Moreover, as Dr. Woodhead has already pointed out, the same substances which in a non-resistant animal repel amœboid cells attract these same cells in considerable numbers when the animal has been artificially protected.

When once the poisons secreted by a particular kind of micro-organism have penetrated into the system, it would appear as if, in many cases, the leucocytes had lost the power of leaving the blood-vessels in order to attack the invading micro-organisms. This loss of power is clearly not always due to a paralysis of the cells, as these still emigrate freely in order to attack certain other bacilli, but results from some other cause still shrouded in mystery.

I must refer to Dr. Klein's theory that the cells in the lymphoid tissues attract micro-organisms, and that "the bacteria find in the cells some attractive chemical substance which suits them, and hence these cells, far from being the enemies of the bacteria, are, on the contrary, their places of refuge for a time at any rate. This view seems to me just as feasible as Dr. Ruffer's view, that because these cells contain bacteria, therefore they are the chief

and only bacteria-destroyers." Dr. Klein supports his views by two series of facts, namely, 1, that in a great many diseases the cells are destroyed by the bacteria, an objection which I have already answered; and, 2, that in a great many bacterial diseases the bacteria are found in the lymphoid tissues of certain organs.

In my lecture, previously referred to, I alluded to the fact that when the micro-organisms are inoculated into an animal the amœboid cells are attracted to the point of inoculation, and that by Dr. Klein's theory it was difficult to account for this phenomenon. In his reply he states that I misunderstood him, and that he referred to what takes place in the internal organs. I am sorry that I made this mistake, but nevertheless my argument loses none of its force; for clearly the phenomena at the point of inoculation must be first taken into consideration, and an explanation given which will reconcile Dr. Klein's theory with the phenomena observed. With regard to what takes place in the internal organs, the only evidence in favour of this theory is that micro-organisms are often found in cells. But I contend that this is not sufficient. Should anyone meet a dead lion and find a lamb inside, he, knowing the habits of the lion, would not conclude that the lamb had taken refuge there. True, after a surfeit of lamb, the lion might die of indigestion, but the chances of the lamb ever getting out alive would be very small. Similarly, knowing the voracious habits of the lymphoid cells of internal organs, before we can accept this theory, observations must be made showing that the bacilli of their own accord force their way into the cells; explanations must also be found for the fact that the micro-organisms perish in the cells in enormous numbers; and lastly, he must explain why, according to Bardach, Sudakewitch, and others, animals normally resistant against a given microbe succumb almost invariably when the spleen is removed.

Remember also that phagocytes exert a distinct choice between two kinds of microbes. They will leave the bacillus of tetanus for the bacillus prodigiosus, and the streptococcus for the bacillus of diphtheria. This is well illustrated in the diphtheritic membrane, where at the surface one can see leucocytes taking in numbers of bacilli, but leaving streptococci almost untouched; with the immediate result that streptococci are often met in the deeper parts of the membrane, and with the remote result that secondary abscesses occurring in the course of diphtheria are

never due to the bacillus of diphtheria, but to some other micro-organism.

The study of the diphtheritic membrane shows the remarkable resisting powers of leucocytes, for although the tissues underlying the membrane are necrosed and dead, the leucocytes have the power of marching in their numbers right up to the bacilli and waging war against them, though many, as I have shown, perish in the fight.

Some investigators, the chief of whom is Dr. Buchner, of Munich, have laid great stress on the bactericidal action of the serum of resistant animals. I may perhaps be permitted to express my great admiration for Dr. Buchner's work and that of his followers, and I am ready to allow that the facts, as stated by Dr. Buchner, are in the main correct; but I am far from accepting the view that the fluids of the living animal play any part in the destruction of microbes in the organism.

In the first place, let us see what happens in animals which have undergone no protective treatment. If the bactericidal action of normal serum has anything whatever to do with the resistance of animals towards a particular kind of microbe, then, whenever the resistance of an animal against a given microbe is great, the bactericidal action of its serum on that microbe should also be marked; and when an animal is not resistant, the bactericidal action of its serum should be feeble, or at least slighter than that of a more resistant animal. A rabbit is not resistant to, and its serum possesses a strong bactericidal action on, the anthrax bacillus; a dog is more resistant, and its serum has no bactericidal action on the anthrax bacillus. We have one exception, that is the white rat, which possesses considerable resistance against anthrax, and the serum of which has a strong bactericidal action on the *Bacillus anthracis in vitro*. But this exception proves the rule, for when the *Bacillus anthracis* is inoculated into a white rat, it thrives at first remarkably well, though it is ultimately destroyed by the animal's amœboid cells. That teaches us another thing also, namely, that it is impossible to argue that those phenomena which occur *in vitro* exclusively take place in the living body.

Were other examples necessary, I would draw attention to the fact that, *in vitro*, the serum of the non-resistant rabbit is a bad cultivating medium for the *Bacillus pyocyaneus*, whereas the

serum of the resistant guinea-pig is an excellent cultivating medium for the same bacillus. And, conversely, I would point out that the serum of the resistant rabbit is an excellent cultivating medium for the bacillus of Chauveau, and that of the non-resistant guinea-pig a very bad medium for the same micro-organism. Moreover I have proved that the fluids of both kinds of animals, when alive, form an excellent cultivating medium for this same bacillus. And yet another example of a similar nature: the bacillus of diphtheria in most animals is only found at the seat of inoculation, and in rabbits and guinea-pigs never spreads any further; and yet the serum of such animals is an excellent cultivating medium for the bacillus of diphtheria.

With regard to Sanarelli's experiments with the cell-free lymph obtained from the frog's lymphatic sac, I must acknowledge that such experiments are extremely interesting, and throw great credit on the scientist's ingenuity; but I contend that, from the point of view which interests us, they prove absolutely nothing.

This gentleman placed particles of organs of an animal dead of anthrax in a small closed collodion bag, from 3 to 4 centimetres in length, and capable of holding about 1 cubic centimetre, and inserted the whole in the lymph-sac of a frog. Three or four days afterwards he removed this bag, and placed it under the skin of another frog; and then, after a like period, under the skin of a third frog. Examining its contents on the eighth or tenth day after its introduction into the lymph-sac of the first animal, he found that no leucocytes had penetrated into the bag, but that the anthrax bacilli were mostly degenerated, and no longer capable of reproducing the disease when inoculated into a non-resistant animal. Now it is almost impossible to introduce a bag measuring more than one inch under the skin of a small animal like a frog without producing not only serious lesions, but without grave risks of contamination also. In Sanarelli's paper there is nothing to show that the fluid bathing the outside of this bag was aseptic. Moreover, when we remember how leucocytes will force their way in a few days into such hard resistant objects as bone and ivory, it is difficult to believe that the inside of these thin collodion bags should have been free of leucocytes. But granting the fluid outside the bag was completely aseptic, and that no leucocytes had penetrated into the bag, I do not allow for one moment that the lymph contained therein was normal, such as that found in living animals.

The lymph during the last days of the experiment was a mixture of three different kinds of lymph, collected during eight or ten days from three different frogs. Were any evidence necessary to show that this lymph was quite abnormal, I would point to Sanarelli's own paper, in which he says that the histological elements of the tissue introduced into the bag were so altered that they were perfectly unrecognisable. Would anyone maintain that normal lymph will destroy such a hard-resisting element as the nucleus of a cell?

Interesting, therefore, as are Sanarelli's experiments, they prove nothing as to the bactericidal action of the normal lymph of a frog.

It has been proved experimentally that after an animal has been artificially protected against a given infectious disease, the serum of such an animal *in vitro* is a bad cultivating medium for the micro-organism causing the malady, and by some this has been set down as a general rule. This is not so, however, for the serum of animals artificially protected against the bacillus of diphtheria possesses no bactericidal action on the bacillus of that disease, and the same remark holds good for tetanus. As I was writing this paper I received a copy of a paper by Mossig, in which he states that the serum of rabbits artificially protected against the pneumococcus is a far better cultivating medium for the pneumococcus than the serum of a normal animal. This bactericidal power of serum is, therefore, not an essential corollary of the increased resistance of artificially-protected animals. Moreover our knowledge of it is at present extremely unsatisfactory, for there is no evidence to show whether it be a specific power of the serum on the micro-organism producing the disease, and on that micro-organism only; and we have no knowledge as to how long the serum of the animal retains this bactericidal power. I have very strong reasons for thinking that it is only of a very transitory nature, passing off long before the animal has lost its increased resistance. However that may be, see what happens when an animal is inoculated with a micro-organism on which its serum exerts its bactericidal action *in vitro*. For I repeat it, what we want to know is not what happens when a micro-organism is introduced into a test-tube together with that wholly artificial substance called serum, but the point is what happens when it is introduced into the living tissues and blood of an artificially protected animal. I may perhaps be pardoned if I again refer to a series of experiments

which Dr. J. H. Walker and I made on guinea-pigs, the resistance of which had been strengthened by a previous inoculation of the *Bacillus pyocyaneus*. We chose this bacillus because my friends MM. Charrin and Roger have shown that the blood of animals artificially protected against this micro-organism possesses strong bactericidal powers.

The guinea-pigs, which naturally possessed a high degree of resistance against this bacillus, had been further protected by an inoculation of 0·25 cubic centimetre or 0·50 cubic centimetre of a virulent culture of *Bacillus pyocyaneus*, and at the time we used them for our experiments they were perfectly recovered, and proved to be efficiently protected against this bacillus. The skin of the animals was carefully shaved, and two drops of a bouillon culture were injected under the skin. This dose does not produce the slightest symptom in protected animals. The first guinea-pig was killed by chloroform *twenty minutes* after the operation, and cover-glass preparations were made from the seat of the puncture and stained with Loeffler's blue. In each slide several leucocytes were found already crammed with bacilli, while a great many micro-organisms were floating in the exudation fluid, and showed not the slightest sign of degeneration. Cultures made from the point of inoculation gave an abundant crop of perfectly healthy and normal bacilli.

Another animal was killed after two hours. Here the leucocytes were already in far greater numbers, and contained numerous bacilli. The micro-organisms floating free in the exudation fluid were absolutely normal, and grew abundantly on agar, gelatine, and bouillon.

Another guinea-pig was examined after six hours, and the point of inoculation was full of multinucleated amœboid cells, every one of which was crammed with bacilli. A large number of organisms were still free, and consisted of short, straight, and extremely motile organisms, which grew abundantly on various cultivating media.

The fourth guinea-pig was killed after ten hours, and presented much the same appearance as the last; whilst in one killed twenty-four hours after the inoculation the leucocytes had emigrated in incredible numbers, and the number of bacilli floating freely in the exudation liquid had correspondingly decreased, although such of them as remained free were marvellously active. A culture was

made from the point of inoculation, and this proved to contain nothing but the *Bacillus pyocyaneus*.

Although the bacilli had remained for twenty-four hours in the living fluids of this doubly resistant guinea-pig, it was impossible to detect the slightest sign that the fluids of the living animal had exerted their vaunted bactericidal action. On the contrary, they proved excellent cultivating media for the organisms.

Further, we found that the cultures made with the *Bacillus pyocyaneus* which had lived for twenty-four hours under the skin of a guinea-pig proved excessively virulent; and in one case, of a rabbit artificially protected and inoculated straight into the veins, we found active and virulent bacilli eight days after the inoculation.

Some observers object to the use of filter-paper for wrapping up the virus, when the object in view is to study the bactericidal action of the fluids of living animals, on the grounds that it may arrest some of the bactericidal constituents of the lymph. It is strange that these gentlemen should bring forward this argument, as they accept the evidence based on serum which has been filtered through a porcelain filter; and it has been the boast of some observers that the bactericidal action of serum could not possibly be due to the cells contained in it, as the bactericidal action was not abolished by passing through porcelain. In fact, these gentlemen strain at the gnat, but willingly swallow the camel. As a matter of fact, however, I showed that leucocytes in a few hours had made their way through the filter-paper into the interior of the bags, and it is clearly impossible to suppose that the same paper, which is unable to arrest leucocytes, should prove an effectual barrier to a chemical substance.

The increase of virulence in the tissues of artificially protected animals is a result which might have been foretold; for if any micro-organisms survive at all in such animals, they must be those which, from some cause or other, possess qualities enabling them to resist the attacks of leucocytes, and to adapt themselves to their new medium. A short time after the inoculation all the weaker micro-organisms must have been destroyed, whilst only the stronger ones survived, and by this process of elimination a more hardy race of bacilli must have been obtained. And do we not see the virulence of anthrax increased by passing through resistant animals, such as dogs and pigeons, and the bacillus Chauveau rendered more virulent by living in the subcutaneous tissues of resistant

animals? But I will leave this point, as most probably Dr. Cartwright Wood will shortly have more to say on this subject, though I must again insist on the fact that in a large number of bacterial diseases, if not in all, there is no evidence to show that the fluids of a living resistant animal have the slightest attenuating action on the micro-organisms causing the disease.

I think there are few pathologists who will not readily confess to the feeling of intense astonishment which seized them when they first read Ogata and Jasuhara's paper, or rather the account of it, as it appeared in the 'Centralblatt f. Bakteriologie.' Everyone had been trying to find a remedy against anthrax, and everyone had failed; and now it was sufficient to inject the minutest drop of a resistant animal's blood under the skin of another animal to cure it of anthrax. True, there were a few points in the experiment which did not appear quite clear, but still the evidence seemed fairly conclusive. Unfortunately, when other experimenters tried to reproduce these results they failed without an exception. But, for the sake of argument, we will suppose that Messrs. Ogata and Jasuhara's results are correct, and that for some reason or other the other experimenters were wrong. Granting all this, even then I do not see how Dr. Klein's contention holds good that the cure of anthrax in these cases may be due to the antiseptic powers of the injected blood.

In the first place, the quantity injected was infinitesimally small, and it was not always injected on the side where the virus was introduced, but occasionally on the opposite side, so that this drop of dog's or frog's serum, before it had the opportunity of acting, was diluted in the whole of the blood of a mouse inoculated with anthrax. Moreover, when we come to see what is the action of dog's blood on anthrax bacilli, we find that it has only a very weak, if any, bactericidal power; so that, if Dr. Klein's opinion be correct, we must suppose that dog's blood, which has normally no bactericidal power, when injected into a mouse suddenly exerts—for reasons not explained—such a strong antiseptic action that it is able to kill millions of bacilli introduced into the mouse's system, although diluted in the whole of the animal's blood.

And what I have said of these experiments applies with even greater force to experiments made with the serum of animals artificially protected against tetanus, which possesses no bactericidal action on the bacillus of tetanus.

Of Mr. Hankin's experiments with the proteid he obtained from the spleen of white rats I cannot speak from the chemical point of view; but one thing seems to me certain, namely, that this action of this proteid cannot be due to any bactericidal powers it may possess. For it is impossible to believe that a dose of albuminoid matter, which has the power of killing a limited number only of spores *in vitro*, should be able to destroy the millions of bacilli introduced into the excellent cultivating medium formed by the mouse's tissues and fluids. May I incidentally enter a protest against the crowd of new names with which Mr. Hankin has lately attempted to saddle our bacteriological vocabulary? To speak of alexines is scarcely scientific, when their very existence is a matter of considerable doubt; but to talk of mycosozin, or mycophylaxin, when we have not the remotest idea what sozins or phylaxins are, or whether there are any such bodies, is hardly pardonable. Surely the first thing to do is not to give a hypothetical body a high-sounding name, but to isolate and study that body.

Truly the bactericidal properties of the serum of artificially protected animals are suggestive, and deserve to be studied. But I maintain that there is no causal relation between the bactericidal properties of the serum of a given animal against a given micro-organism, and the acquired resistance against the same microbe.

One of the speakers has referred to the experiments of Behring, Kitasato, and others, according to which the blood of an animal artificially protected against a given microbe possesses the property of destroying the poisons produced by that microbe, not only *in vitro*, but also in the tissues of the living animal; and some have gone so far as to say that it was to this poison-destroying power of the serum that the increased resistance of such animals was due. Far be it from me to depreciate in any way the important results obtained by Messrs. Behring and Kitasato, but at the same time it is evident that this poison-destroying power of the blood is not a necessary accompaniment of the increased resistance of such animals. Thus fowls possess considerable resistance, not only against the bacillus of tetanus, but even against the poisons secreted by this bacillus; and yet the blood of fowls possesses no action whatever on the tetanus poisons. Let us turn now to animals artificially protected. Undoubtedly the serum of a rabbit protected against tetanus often possesses the power of destroying the tetanus poisons, but this is by no means *always* the case; and

yet the rabbits, whose serum does not destroy the toxines, possess an increased resistance against the bacillus.

We must conclude, therefore, that although in artificially protected animals this property of the serum may be noticed, yet it may be absent even in protected animals, and is generally wanting in animals naturally resistant against tetanus; and also that the increased resistance of such animals is not primarily dependent on the poison-destroying power of the serum and tissues.

Another point which has been mentioned is that animals artificially protected against a living microbe can also to some extent resist the poisons of that microbe. Undoubtedly this is occasionally the case, but it is by no means a general rule, nor is this property of being able to resist poisons a necessary corollary of the increased resistance of animals artificially protected. Quite the reverse, in fact; for in some cases artificially protected animals have less resistance towards the poisons than non-protected animals of the same species. It is occasionally possible to render animals insusceptible to the poisons of the vibrio Metschnikovi, but usually those animals which are already resistant against the vibrio succumb to the action of poisons more easily than non-resistant animals.

Similarly with the *Bacillus pyocyaneus*. Some observers have occasionally been able to protect animals against the poisons of the *Bacillus pyocyaneus* but in most cases they have failed, although the animals had gained an increased power of resistance. I found, for instance, that by injecting small doses of sterilised cultures at varying intervals the animals invariably died, whilst a few small doses markedly increased their resistance. The conclusion to be drawn, therefore, is that the power of resisting bacterial poisons is not a necessary accompaniment of immunity, but may be present or absent without apparently influencing in any way the resistance of animals.

There is only one class of cells which appear to possess the power of quickly becoming accustomed to bacterial poisons, namely, the cells which are designated under the term of phagocytes. No doubt means will be found to increase the resistance of other cells of the body to bacterial poisons, and far be it from me to say that such an increased resistance, and the poison-destroying power of the blood and tissues of the body, do not play a part in reinforcing the resistance of animals; but I maintain that at first this

property is not a necessary accompaniment of the increased resistance of animals.

It has been proved that the injections of bacterial poisons so influence the cells of the body that, long after their introduction, marked changes take place in the various organs of the body—changes which often prove fatal to the animals. But no doubt the converse is true; and in other cases the changes are of such a nature that they are of assistance to the cells in resisting the action of micro-organisms and their poisons. That is a notion which is as old as the notion of micro-organisms as essential factors in the production of disease.

There are many other points which I would have liked to touch upon, more especially the evidence of the so-called immunity produced by the blood of so-called immune animals. I must leave this for a future occasion, but I may state at once that these experiments, should they prove correct, are capable of quite another explanation than that given by their authors. And may I remind the Society that, more than two years ago, Dr. Charrin and I proved the presence of the poisons of the *Bacillus pyocyaneus* in the urine of artificially protected animals fourteen days after these poisons had been introduced; and also that we succeeded in rendering rabbits resistant by the injection of the blood of animals suffering from the pyocyanic disease? The explanation we gave of this phenomenon was a good deal simpler than that now offered us; but we forgot to coin half a dozen Græco-Latin words in connection with it, which circumstance may perhaps account for the fact that our discovery has fallen into oblivion.

In conclusion, it is my firm conviction that the only process which has been proved to be essential to the resistance of animals—whether this resistance be natural or obtained by artificial means—is the power that amœboid cells possess of taking into their interior and destroying micro-organisms; and that there is overwhelming evidence to show that this process is proportional to the resistance of the animal. Finally, let me again repeat that neither Metschnikoff nor any of his pupils have ever said that this was the only cause of natural or artificial resistance.

Mr. C. A. Ballance.—I am afraid I have nothing new to say, but I understand from the authorities that this need not prevent me from taking part in this discussion. There is one reason, at

least, which prompts me to do so, and that is that no surgeon has as yet contributed to the debate. It has always seemed to me that the question of immunity has an especial and weighty interest for surgeons, since our daily occupation is the making of wounds, which, if they are not rendered immune against the attacks of micro-organisms, may seriously imperil life. This immunity is attained as the direct outcome of the actions of the living cells and fluids in the neighbourhood of the wound. The surgeon can only aid the natural processes by employing means calculated either to prevent the entrance of, or to destroy, or to inhibit the action of, those deleterious things which can thwart the struggle of the injured tissues towards the attainment of immunity. The healing of the body against the more generalised specific diseases is, I think, comparable with the processes employed by nature in the healing of wounds. The presence of pathogenic micro-organisms or their poisons in the body constitutes, in one sense, really nothing more than the presence of a foreign body, which it is the function of the natural processes to get rid of. The observation, then, of the manner in which nature can absorb and remove foreign material in wounds will to some extent aid us in the study of similar processes when engaged in warfare against disease. It is not to be supposed that the tissues are supplied with various weapons, each designed to repel the attack of a different foe; but we may take it, I fancy, that the armour of the body and its weapons of offence are alike, whatever be the foreign matter which has to be dealt with.

I do not, therefore, propose to refer to any of the classical researches which have been so largely drawn upon by previous speakers, but to make some plain remarks on the healing of wounds, and to see how far light may in this manner be thrown upon the following questions:

1. When a part is invaded by cells in consequence of the presence of a foreign body, solid or liquid, living or dead, are there one or two distinct kinds of cells which participitate in the invasion, or is it true, in other words, that only a leucocytosis occurs?

2. If there are two distinct kinds of cells whose mission it is to invade the tissues under these circumstances, which kind is the most vigorous, and is the most effective agent in the protection of the body against disease?

3. What, if any, effect have the cells during periods of rest or

activity on the constitution of the fluids in which they dwell? in other words, whence comes the antitoxic or defensive substance which the humoralist alleges is present in a fluid, or fluids, of the body?

Professor Sherrington and I, in studying the question of repair, introduced small Ziegler chambers into the subcutaneous tissue and peritoneal cavity of certain animals. In the chambers, in the tissue around the chambers, as well as in the normal tissue and plasma, and normal peritoneal moisture, we found two distinct kinds of cells. The one kind résembled in all respects the leucocyte—the colourless corpuscle of the blood; the second kind was much larger, 30 μ to 40 μ across, and possessed a large oval vesicular nucleus (itself larger than a red disc), which stained faintly (not deeply, like the nucleus of a leucocyte), and the protoplasm of the cell body was markedly granular. The examination of the specimens took place on the warm stage, and also after fixation with osmic acid.

Both these kinds of cells migrated into the chambers, but there was a definite sequence of events, the leucocytes commencing to enter the chamber shortly after it was implanted in the body, whilst the larger corpuscles (which section of the inflamed tissue around showed to be the daughter cells of the surrounding connective-tissue corpuscles) did not commence to invade the chamber until some eighteen hours had passed.

Briefly, the subsequent events observed were a loss of vitality of the small kind of cell, and its inclusion in the vacuole of the larger kind. The larger kind, when all available food in the shape of fibrin and blood-corpuscle had disappeared, commenced to lengthen out and spin fibrous tissue; much as Amœba under adverse conditions assumes an encysted form, so when food is scarce do the inherited tendencies of the amœboid connective-tissue cell lead it into the state of quietude and encystment. The less nutritious, the more inert, the foreign body, the sooner do the amœboid tissue-cells become fixed. In the same specimen in which these cells, still actively amœboid, were preying upon blood-clot, it often happened that around innutritious matter, as hairs, cotton fibres, particles of shellac-glue, &c., the cells were perfectly developed into young connective tissue.

I should like here to add that we were greatly assisted in the interpretation of the appearances seen in the osmic fixed prepara-

tions by the processes described by Miss Greenwood in the Rhizopoda. Her observations were conducted on living specimens of *Amœba proteus* and *actino-sphærium*, and she was able to follow under the microscope all the visible phenomena of the ingestion of prey. In our experiments we had a number of amœbæ, many of them actively engaged in ingesting living prey at the moment that the reagent employed killed them. Just as in the interesting observations of Miss Greenwood little monads Englenæ and Algæ co-existing in the same water as *Amœba proteus* were by it ingested, so the leucocyte becomes the prey of the amœboid connective-tissue cell. Of Amœba and Actino-sphœrium it was found that the fluid in the food vacuole was most active upon, and therefore that the food most suitable for these forms was unshielded, non-coagulated, proteid matter. Our connective-tissue cell is a hothouse variety of amœba, and finds its unshielded, non-coagulated, proteid food in the dying leucocyte; for a low degree of activity renders an organism an easier prey, with less difficulty captured and more readily absorbed.

In the chambers we observed giant-cells formed by the fusion of connective-tissue cells, or by nuclear multiplication without actual separation of the daughter cells from the parent. These giant-cell forms seemed especially to be present when the substance to be absorbed was more resistant than usual.

We arrive, then, in this way at the conclusion that the invading leucocyte has only a temporary purpose to fulfil in the healing of a wound; and we are justified, I believe, in thinking that the number invading the tissues is to some extent adapted to the nutritive requirements of the amœboid connective-tissue corpuscles, whose food they constitute, and which alone spin the connective tissue that repairs the wound.

The rush of leucocytes which occurs towards a spot invaded by micro-organisms may be thought of as useful in various ways.

1. Though of feeble vitality they may be able to digest and destroy certain of the foreign organisms;

2. By the death of others a ferment may be set free which may diminish the vitality of some of the bacteria, and thus cause them to be an easier prey of other cells; and

3. Abundance of food (in the shape of leucocytes) for the after-coming connective-tissue corpuscles will be associated with the attainment by them of the highest degree of vigour and vitality.

All the main work, then, in wounds, not only with regard to repair, but with reference to the removal of foreign bodies such as clot, ligatures, micro-organisms, &c., falls upon the connective-tissue cell.

In passing I may mention that our observations give no countenance to the old Cohnheim doctrine of the development of leucocytes into connective-tissue cells; the connective-tissue cell was distinguished by its larger size; its coarser granules; its single, clear, oval, vesicular nucleus; its staining qualities; its permanence as compared with the perishability of the leucocyte; and, lastly, by the period at which it commenced its voyage into the inflamed area.

"The legitimate succession of cells is now a well-established law in pathology as well as in embryology, and, according to this, tissue is never produced by substitution of function. No positive proof has yet been furnished that the elements of the blood take any active part in the restoration of lost parts. It does not appear to me reasonable or logical that such an indifferent cell as the leucocyte should ever become transformed directly into a fixed tissue-cell, and it is still more improbable that it should be possessed with such a diverse vegetative capacity as to undergo a transition in one place into a connective-tissue cell, in another into bone, and still another into muscular fibre."

If it is argued that leucocytes are produced from lymphatic tissue, and that therefore they may change into connective-tissue corpuscles, the reply is conclusive that lymphatic tissue is as special and differentiated as either muscular or nervous tissue, and no one alleges that a muscle-cell can produce nervous tissue. Then why, it may be asked, should a lymph-corpuscle be supposed capable of spinning a connective-tissue fibril? It must be remembered that the supporting framework of lymphatic, nervous, and muscular tissue is connective tissue, hence in all these parts connective-tissue corpuscles are found.

Other facts against the view that the leucocytes are tissue repairers are—

1. That in health they have but an ephemeral existence.

2. That in old clot in aneurysms no connective-tissue growth occurs unless the coagulum becomes adherent to the aneurysmal wall, and so becomes capable of being invaded by the tissue-cells.

3. That repair in the vegetable kingdom is carried out entirely by the fixed cells of the part injured.

4. That the whole story of the normal life of the leucocyte is that of ceaseless change of form, which is incompatible with the spinning of a semi-solid test around itself, which, on the other hand, is characteristic of cells of connective-tissue origin.

If, then, the leucocytes in the healing of wounds have a subordinate function to fulfil, is it not probable that they also have a subordinate place in the fight against disease, and in the attainment of a state of either natural or acquired immunity?

Bacteria, whether pathogenic or not, are carried to certain definite situations when injected into the blood, namely, to the spleen, liver, kidneys, bone marrow, &c., where they can be acted upon by tissue-cells, and notably in the spleen and bone marrow by the giant-cells there located. Poisons in solution, too, appear to be collected in the same situations, it may be for a similar purpose, namely, to be acted upon by the tissue-cells. In both instances the leucocytes may be the carriers to the tissue-cells, or these special regions of the body may perchance have some special power of separating poisons, particulate or in solution, from the blood. In this relation it is interesting to note that certain proteid substances in solution in water (*e. g.* acid and alkali albumen) will not pass through a porcelain filter.

Again, in the formation of an abscess it is not the leucocytosis to the part which arrests the disease, but the wall of connective tissue formed around the infected spot by the after-coming connective-tissue corpuscles.

I think, then, we may believe that the presence of the connective-tissue corpuscle, a cell having a definite permanence in the tissue as compared with the perishability of the leucocyte, must be of prime importance in the conflict with bacteria and bacterial poisons.

The amœboid cells of the body we have observed devouring in their food vacuoles various kinds of food and various foreign material. The further question now arises, what action have they upon substances outside themselves; in other words, do they give to the fluids they live in a material or ferment which can act upon uncoagulated, unshielded proteid in the same way as does the fluid of a food vacuole? That this is so is shown by many facts, a few of which are as follows:

1. The outline of the cells of clot which is invaded by tissue-

corpuscles is lost often before the invading cells actually touch them, and the appearance is quite different from the change which occurs to the cells of old uninvaded coagula.

2. Resistent foreign bodies could not be absorbed unless this were so. It is well known that encapsulation does not arrest absorption.

3. All the known ferment manufacturing cells pour their secretion into the world outside themselves, and why should not the leucocyte and the connective-tissue cell do the same when imperatively called upon to attack a foreign body?—just as gastric cells do when called upon to change an insoluble proteid into soluble peptone.

4. The osteoclasts of bone during the process of ossification cause absorption of the primary areolæ. The same thing occurs in rarefying ostitis. On the warm stage proximity to a connective-tissue corpuscle diminished the activity of a leucocyte, and Miss Greenwood says that sluggishness induced by dying allows enclosure, and that quiescence on the part of a motile prey occurs previous to determinate ingestion.

These facts show an influence of the animal cell on the world outside itself; and, indeed, it is not to be supposed that a cell would shed into its food vacuole a ferment which would not also be given off by the general surface of the protoplasm. Thus we may explain the alleged bactericidal power of the body fluids. It must be remembered that vacuoles are only present during a state of high functional and digestive activity, but I fancy there may be always going on a consumption of amœboid leucocytes by those few connective-tissue cells which are normally free. The poor we have always with us, and so have we the leucocytes, but it is only in times of danger that the tissue-cells can be found in large numbers active and mobile, and thus we may possibly overlook the *rôle* they play. The death of leucocytes, which is always occurring, might be thought of as setting free into the body fluids fibrin ferment, and fibrin ferment (if it exists) must be closely allied to Hankin's antitoxic substance and Wooldridge's tissue-fibrinogen. Clearly, whatever is in the fluids of the body must come from the cells. The normal physiological activity of the cells of the body may thus possibly explain the defensive action of the healthy tissues and fluids against bacterial infection. This clearly exists, for to produce disease a definite dose of micro-organisms must be administered. The normal quantity of antitoxic substance present during

any given period may perhaps correspond to the quantity of antitoxic substance (query—a proteolytic ferment?) present in the food vacuoles + the quantity secreted from the surface of the cells into the surrounding fluid. If, on the other hand, it were proved that living serum and plasma are not bactericidal, it would follow that the antitoxic substance must be a weapon only used under conditions of irritation or emergency by the cell. It may be that an increase in normal physiological activity of the cells, acquired as a habit, may explain, to some extent at least, some of the varieties of immunity.

In conclusion, I desire to express the opinion that, however beautiful the researches may be that are conducted by the aid of the microscope alone in revealing more of the activity and life of cells, yet we shall not in this way progress far on the road towards a true knowledge of the intimate pathology of immunity. The problem of immunity is essentially a chemical one, and its solution must be sought in the laboratory of the chemist.

Mr. E. H. Hankin.—I have elsewhere expressed the opinion that the bactericidal power of normal blood-serum is acquired as the result of some *post-mortem* change, and that no such power is possessed by the fluids of the living body in the normal condition. I have also suggested that the serum acquires its bactericidal power in consequence of the liberation of bacteria-killing proteids, or alexins, which are freed from the cells on the death of the animal.

In the present communication I propose to discuss certain points connected with the chemical nature of alexins.

In the first place, it has been objected (by Buchner and others) that alexins have not been prepared in a state of purity, and that consequently they cannot really be said to have been *discovered* in the ordinary sense of the word. Usually a substance is said to have been discovered when it has been obtained in a crystalline form, its boiling or melting point observed, and its chemical constitution at least approximately determined. None of these conditions have been fulfilled in the case of alexins. How, then, can they be said to have been discovered?

To state that alexins belong to the class of ferment-like proteid bodies at once diminishes the poignancy of this criticism to any physiological chemist. No one would deny that fibrin ferment has

been duly discovered, although chemically its characters can for the most part only be stated in negative terms. Further, as I shall proceed to show, far more is known of the chemical characteristics of alexins than of fibrin ferment.

In nearly every paper that I have published on this subject I have stated that alexins (and here I am especially referring to those of the normal animal) are identical with a substance discovered by Halliburton, and termed by him cell-globulin β.

Halliburton carefully worked out the chemical characters of this substance, and at the time of its discovery believed that it was identical with fibrin ferment. At the time referred to (about two years ago) certain facts discovered by Buchner relative to the bactericidal power of blood-serum suggested to me that this bactericidal power was due to the presence of a globulin allied to fibrin ferment. Experiment soon showed me that Halliburton's cell-globulin β possessed this power, and so differed from the classical fibrin ferment of the physiologists.

Halliburton found that a one tenth saturated solution of sodium sulphate has the property of extracting this cell-globulin β from the cells of lymphatic glands in a state of comparative purity. Only traces of other proteid bodies are extracted with it by means of this solvent. Halliburton also showed that cell-globulin β differed from other globulins (and resembled fibrin ferment) in not being rendered permanently insoluble by the action of alcohol. In the method of preparation of alexins that I have employed I have taken advantage of these two facts. I have first made an extract of the spleen or lymphatic glands with the dilute sodium sulphate solution, and then precipitated it with a large quantity of absolute alcohol, with the idea of permanently coagulating the traces of other proteids present. On extracting the alcohol precipitated proteids with water I have thus obtained solutions of alexins probably in a state of greater purity (so far as the presence of foreign proteids is concerned) than is usual when dealing with substances of this nature.

These considerations have led me to devote my attention to the relation of alexins to immunity, and to leave any further study of their chemical characters to the physiological chemists. Dr. Wright's contribution to this discussion on immunity, however, impels me yet further to discuss this side of the subject.

In the communication referred to, Dr. Wright states his opinion

that alexins are identical with the tissue-fibrinogen of Wooldridge. If this is the case, my work on alexins must be regarded as a contination of Wooldridge's interesting and well known work on immunity against anthrax produced by means of tissue-fibrinogen. Dr. Wright has treated the subject with a greater degree of "cocksureness" (if I may use the term) than would, I think, have been the case had he done me the honour to make himself better acquainted with my published papers. As I have heard the opinion of the identity of tissue-fibrinogen with alexins supported by others, with a warmth not at all proportional to knowledge, I think it advisable to give in detail my reasons for holding the contrary opinion.

In doing this I am confined to stating the differences between alexins and tissue-fibrinogens. Resemblances between these two groups of bodies are, so far as our present knowledge extends, nonexistent, except such as they hold in common with other proteids.

(1) Wooldridge, by means of tissue-fibrinogen, succeeded in producing a lasting immunity against anthrax; perhaps, indeed, I should describe his experiments as resulting in a cure of the disease. The alexins obtainable from normal animals will not (so far as my experiments go) either "cure" a disease or produce immunity.[1] It is well known that tissue-fibrinogen has not the power of destroying anthrax bacilli. The alexins with which I have worked, on the other hand, do so.

(2) Tissue-fibrinogen causes clotting when added to peptone plasma, but not when added to magnesium sulphate plasma. An alexin solution, on the other hand, clots magnesium sulphate plasma, but has no visible action on peptone plasma. That is to say, alexins and tissue-fibrinogens exhibit exactly opposite properties when tested on these two kinds of plasma.

(3) Wright states that my method of preparing alexins is a perfectly ideal way of obtaining tissue-fibrinogen. The chief property of a tissue-fibrinogen solution is its power of producing intravascular clotting. We have yet to learn than an alexin solution prepared by the method in question possesses this power. Ob-

[1] The alexin of the rat when mixed with anthrax spores and injected into mice will generally prevent the development of the disease. This is obviously not a case of "cure," still less a "permanent immunity." It is nothing more than an inhibition of the development of the disease, depending on the local action of the serum or alexin solution.

viously, however, traces of tissue-fibrinogen might be present, as Wright suggests. How, then, is it possible to prove that the special activity of an alexin solution is not due to such traces? This proof can be readily obtained by what is known as the method of concomitant variations. If we take a series of liquids of different origins containing different quantities of tissue-fibrinogen, we might expect that those liquids that contained most tissue fibrinogen should have most action on bacteria, supposing the tissue-fibrinogen to be the active principle. That this is not the case is shown by an examination of the following series:

(*a*) Solution of tissue-fibrinogen prepared by Wooldridge's method.

(*b*) Watery extract of the thymus.

(*c*) Watery extract of the spleen.

(*d*) Alexin solution prepared by my method.

(*e*) Blood-serum of the rabbit.

The first three liquids mentioned contain large quantities of tissue-fibrinogen, but exert no bactericidal action. The next on the list admittedly contains tissue-fibrinogen only in traces, if at all, yet it has a decided action on bacteria. Lastly, no one would, I think, venture to suggest that blood-serum of the rabbit contains any tissue-fibrinogen at all, yet it exerts a stronger bactericidal action than is, as a rule, possessed by alexin solutions that I have been able to prepare.

The serum of the dog is, as Wooldridge has shown, more or less exceptional in that it contains traces of fibrinogen. This is, however, a substance having very different properties from tissue-fibrinogen, and Wooldridge has termed it "serum fibrinogen." The serum of the dog is also exceptional in the feebleness of its bactericidal power. According to several authors it has, as a rule, no action on the anthrax bacillus. But, further, the following consideration gives a reason for thinking that some at least of the alexin solutions that I have prepared did not contain a trace of tissue-fibrinogen, but rather an impurity of quite a different nature. Alexander Schmidt has recently shown that if various organs (especially the lymphatic glands) are extracted with alcohol immediately after death, and the residue then extracted with water, a solution is obtained having properties exactly the converse of those possessed by tissue-fibrinogen. This solution contains a substance termed "cytoglobin," which has the property of pre-

venting or delaying the coagulation of the blood. This property is shown when it is allowed to act on the blood either before or after the removal of the latter from the body. We see, then, that various organs after exhaustion with alcohol are no longer fitted to yield tissue-fibrinogen, but, on the other hand, can furnish a substance having a converse action on extra- or intra-vascular blood. Now in many cases I have washed spleens and lymphatic glands with alcohol before extracting them with sodium sulphate to obtain an alexin solution. In the solutions thus obtained very possibly traces of cytoglobin were present. Nevertheless their bactericidal action was often better marked than in solutions obtained from glands that had not previously been treated with alcohol. Further, I have observed in one experiment that a solution of cytoglobin prepared by Schmidt's method showed a very slight bactericidal power.

It is, I think, generally admitted by physiological chemists that tissue-fibrinogen is not a single substance, but a complicated mixture of globulins, nucleo-albumens, and possibly of alexins and other proteid substances. To whatever substance or substances the chief properties of a tissue-fibrinogen solution are due, and whatever the chemical nature of alexins may ultimately turn out to be, there is plenty of reason for thinking that they are extremely different physiologically, though they may be closely related from the chemical standpoint.

(4) In the case of the rat we obtain a very simple and clear proof of the non-identity of its alexin and of its tissue-fibrinogen. I have elsewhere shown that the alexin of the rat possesses an alkaline reaction. This is a striking phenomenon, and perfectly easy to demonstrate. If a solution of this alexin is dialysed against distilled water the alkaline reaction vanishes, because the removal of the salts has caused its precipitation. If now some solid sodium chloride is added the alexin again passes into solution, and the alkaline reaction reappears. The tissue-fibrinogen of the rat does not show any such reaction. Further, the alexin of the rat is permanently destroyed by acidulating its solution. The tissue-fibrinogen of the rat, on the other hand, can be precipitated by acetic acid, and on re-solution in dilute potash again exhibits its characteristic properties.

Before leaving the subject I should like to mention a point where Wright has been particularly unfortunate in his criticism of

my work on alexins. He represents me as having asserted that I could obtain the alexin from tame, not, however, from wild rats. There is every reason for thinking that tissue fibrinogen could be prepared from wild rats as well as from tame ones. Nevertheless Wright suggests that possibly the spleens of the wild rats that I had worked with contained less adenoid tissue than the others, and that consequently I was unable to isolate from them enough tissue-fibrinogen to obtain the reactions characteristic of the rat's alexin. This suggestion is not supported by experimental evidence.

It is not the only case in which I have had occasion to notice that good criticism bears traces of a study rather than of a laboratory origin.

In this case, however, Dr. Wright's ingenuity is misapplied, for he has slightly misunderstood my original assertion. I found that wild brown rats when freshly caught and presumably in a state of good health, or if kept in captivity and fed on a flesh diet, yield as much alexin as white or piebald rats. It is only when they are kept in captivity for some time and fed on a "slop diet" of bread and water that they become easily susceptible to anthrax, and that the alexin vanishes from their spleens. Curiously enough, when in this condition, the alexin can still be found in the blood-serum, apparently in undiminished amount, and, as I have no doubt Dr. Wright will admit, free from admixture with tissue-fibrinogen.

Dr. Ruffer, in his extremely able contribution to this discussion, has expressed certain opinions alike uncomplimentary to my scientific ability and to the results of my work. For instance, he states that the existence of alexins is still a matter of doubt, and consequently that I am unscientific in having suggested for them a classification and a nomenclature. Dr. Roux, in his contribution to the discussion on immunity at the International Hygienic Congress, when referring to my work, stated that it was certain that solutions of proteid bodies having a bactericidal action could be prepared. Metschnikoff, in a review published in the 'Annales de l'Institut Pasteur' in August, 1891, alluded to my proposed classification of alexins in terms very different from those employed by Dr. Ruffer. I have no doubt that Dr. Ruffer will see that in thus quoting the opinions of other bacteriologists I am not giving any scientific proof of the correctness of my views, and consequently he will excuse my taking any further notice of his strictures until he supports them by experimental evidence.

Dr. WOODHEAD.—As I am allowed to say a few words before our President sums up this very interesting discussion, I take the opportunity of drawing attention to one or two points to which I think sufficient prominence has not been given, and on which I think much work has yet to be done. First as to immunity. We are in the habit of looking upon immunity as something absolute and definite, and we speak of an animal as being naturally or artificially immune against the action of certain bacteria, as though it were absolutely protected against the action of these organisms. In one way we are perfectly right; in another we are absolutely wrong. An animal may be so far protected by inoculation that it may resist the attacks of micro-organisms that can find their way into its system by the ordinary channels, and by what we may speak of as natural means, but it has not yet been definitely proved that an animal can ever be fully protected against the attacks of the experimenter who may wish to produce a specific infection. He (the experimenter) has at command at least half a dozen ways of obtaining his end. For example, he may introduce large quantities of the specific organism, or of the toxine formed by this organism into the animal, or he may inject a virus which has been rendered exceedingly active by special preparation or by special methods of cultivation on ordinary nutrient media or in the fluids of living animals. We have a good example of this latter method in the experiment in which portions of a weakened anthrax culture placed in a sponge and introduced into the tissues of a dog become markedly increased in virulence; it is found that when the sponge is removed after several days the anthrax bacilli, which before were capable of killing a rabbit only after the lapse of a very considerable period, have now the power of causing its death in from twenty-four to forty-eight hours. Again, we may introduce the virus into tissues or cavities which normally are never reached by the accidental methods of infection, in which even minute doses of virus are able to set up the disease, doses which, when introduced under normal conditions, would not produce the slightest effect. Lastly, some organisms have their virulence greatly increased when they are grown alongside other organisms, in some cases in artificial nutrient media, in others in the tissues. We have an admirable example of this in Roser's experiments on the effect of the inoculation of the *Bacillus prodigiosus* along with erysipelas streptococcus, and Valliard and Vincent have noted the same thing

in connection with the inoculation of the *Bacillus prodigiosus* along with the tetanus bacillus; it had also been previously observed in *charbon symptomatique*. It has been offered as an explanation of these facts that in such cases we have a cumulative action of the products of these micro-organisms; it has also been explained on the assumption that the cells of the tissues are so occupied in dealing with the comparatively innocuous organism that none of their energy is left to enable them to cope with the more virulent species, which being allowed to act unopposed, sets up its characteristic pathogenic effects, with the result that the patient succumbs.

Those who have worked with anthrax, typhoid, and tubercle will readily call to mind instances of the conditions above mentioned, whilst smallpox and scarlet fever also afford examples of the truth of some of the statements. As we have heard, the dog is said to be immune against anthrax bacillus, but by working with virulent anthrax, and by introducing it under the skin with certain precautions, a very large proportion of the animals may be killed. Rabbits and guinea-pigs are resistent against the typhoid bacillus unless this organism be exhibited in enormous quantities; whilst during the last few weeks I have again had opportunity of determining what an enormous difference there is between the alimentary tract and the peritoneal cavity as regards liability to infection, where only a few partially devitalised tubercle bacilli are present. In the one case we have resistance at the point where the tubercle bacillus is introduced naturally, in the other—the seat of artificial infection—there is extreme susceptibility.

The next point on which it appears to be necessary that we should insist very strongly, is the specificity, within certain limits, of immunity, a specificity recognised by the clinician, but not always by the experimenter. This lack of recognition on the part of the experimenter is, I believe, closely associated with the point to which I have already referred; and in connection with this fact the experimenter must remember that there is a possibility of his being led to draw conclusions which can never be of use under ordinary circumstances to the physician. Upon specific protection Metschnikoff bases his whole theory of phagocytosis.

Coming now to the main question at issue—in connection with which such able contributions have been made in support of the phagocyte theory, of the humoral theory, and, shall I say also, of the intermediate theory?—one cannot but feel that the amount of

direct evidence brought forward bears an exceedingly small proportion to the multiplicity of arguments based on it; but I frankly confess that, so far as I can judge, what little evidence has been adduced has been against the humoral theory, and when I speak of the humoral theory I mean the theory in which is involved the presence of specific poisons in the fluid elements of the blood. Of course, everyone must acknowledge that the fluid elements of the blood can only be what they are made by the living protoplasm of the cells, both fixed and migratory. It may also be freely admitted that as soon as these fluid elements are removed from their normal surroundings they probably rapidly undergo such marked changes that they acquire an exceedingly powerful bactericidal influence—an influence, however, in no way specific, and therefore not associated with specific protection. It may, of course, be objected that it is a difficult matter to obtain positive evidence of the presence of dead bacilli in the blood-plasma, and that, for purely physiological and anatomical reasons, it is much easier to demonstrate their presence in leucocytes; but that does not alter the fact that in the one case we have positive evidence that living as well as dead bacilli have been found in leucocytes; that cultures have been taken from bacilli that have been taken up into these cells; whilst the only proof that we have bacilli in the fluid is obtained from artificial cultivation experiments, in which, of course, the conditions are very different from those that obtain in the living body.

Let me, for a moment, draw your attention to an experiment recorded by Pflüger, for reference to which I am obliged to Dr. Wright, which shows how very early changes take place in the blood when it is shed.

If when peroxide of hydrogen is injected slowly into a vein, the marginal vein of the ear of a rabbit, say, great care being taken that there shall be no escape of blood when the needle enters and is withdrawn, the injection appears to have little or no effect on the health of the rabbit, which goes on feeding and remains perfectly well, so far as we can determine by any rough methods of examination; peroxide of hydrogen then injected into the *living* blood is gradually broken down, and its constituent elements are absorbed. If, however, the smallest drop of blood be allowed to escape into the tissues when the injection is made, and if this blood becomes mixed with a drop of peroxide, there is immediately an evolution of gas, which is not now confined to the point where the blood has

escaped, but extends along the whole vascular area into which the peroxide has found its way, and the animal dies, exhibiting all the symptoms associated with the injection of air into the veins. The living blood is able to deal regularly and systematically with the peroxide, but in the dying blood we have probably rapid escape of gases with alteration in the arrangement of the molecules of the proteid and other constituents, some of which, in a nascent condition, readily unite with the loosely bound-up oxygen of the peroxide; this, having once begun, goes on rapidly, and we have a progressive and continuous reaction as far as the peroxide reaches, like that set up when a train of gunpowder is fired. Such an experiment as this indicates that the molecular arrangement of the blood, though stable enough in the body under ordinary conditions, is extremely unstable under abnormal conditions and when it is removed. Here the nascent molecules may readily unite with the highly organised and somewhat unstable protoplasm of bacteria, which protoplasm may thus be rendered more or less inert.

Let us come now to certain points raised by those who have taken part in this debate: First, as regards Dr. Klein's ingenious experiments on the frog, it certainly does not appear remarkable that where such enormous numbers of bacteria are thrown into the lymph-sac they should readily find their way into the circulation; but it does not follow because they then begin to disappear from the blood and rapidly decrease in number, that they have been killed off by the blood-plasma. To die of starvation and to die of poisoning are two very different things, and it is a well-known fact that the serum of frogs' blood, especially at the temperature at which a frog usually lives, is not a good nutrient medium for the anthrax bacillus; whilst it must also be remembered that as the blood passes through the capillaries, the bacilli are rapidly filtered out, and would, therefore, after a time, not appear in the heart, especially as the anthrax bacilli are apparently not undergoing proliferation. Dr. Klein's objection, too, that the bacilli actually invade the leucocytes in order that they may get out of the way of the germicide in the plasma will scarcely hold for a moment if we take for our example such an organism as the tubercle bacillus, or even the anthrax bacillus, both of which are absolutely non-motile, and have therefore no power of making their way into the protoplasm of an amœboid cell; to carry Dr. Ruffer's simile a little further, we should scarcely expect a paralysed lamb to be found in

the stomach of a lion without some little effort being made on the part of the latter animal.

As regards the propriety of basing our arguments on test-tube experiments, sponge experiments and the like, there can be little doubt that those experiments that are carried on under conditions most nearly approaching the normal are those to which we should attach most value, and therefore I maintain that all experiments with blood-serum are absolutely valueless as giving any indication of the process going on in the blood itself. There is no such thing as blood-serum within the vessels; it is something which is only obtained from dead blood, and therefore can afford us no guide as to what goes on in the body. Very serious objections undoubtedly may be urged against experiments with sponges, paper bags, pith, and the rest, but it must be remembered that these experiments should, according to the opponents of the phagocyte theory, give the strongest evidence of the bactericidal power of the fluid elements of the blood, which certainly cannot be so much altered in their passage through a fragment of sponge as they can in the process of coagulation. Outside the body we can only have serum; within it may be plasma, though altered. As a matter of fact, we find that organisms contained in a sponge, and to which leucocytes have not as yet gained access, instead of being killed off, usually increase in number, even in an immune animal, and very often also increase in virulence (*vide supra*), it may be through survival of the fittest—natural selection. It is contended that the fluid is not in the condition in which it is ordinarily found in the body, but we cannot suppose that all the large quantity of fluid that passes over and through this little bit of sponge can be altered immediately it comes in contact with it, or we should very soon have a large proportion of the fluid in the body undergoing the great changes that are said to take place at this point, a condition that could only be attended with serious consequences to the patient. Mr. Kanthack mentioned Sanarelli's experiments, and very properly objected to the conditions under which they were performed, but these experiments have been quoted in support of the bactericidal power of the lymph from the dorsal sac of the frog. As Dr. Ruffer has pointed out, there are initial objections to these experiments as to the method in which the tubes are kept and filled, and the consequent risks of mixture of organisms, septic inflammation, and the like; but there is a far more serious objec-

tion than any of these; these tubes are made of celloidin, one of the most perfect dialysing membranes with which we are acquainted. Now, from what we know of the composition of blood, can we expect to find in a fluid obtained by dialysis anything more than a mere trace of the proteids ordinarily present in the blood? Any small quantities of peptones, albumoses, and the like that may be in the blood may pass through in certain proportions, and from the changes set up as the result of the inflammation, it is probable that a larger proportion than usual of such proteids, globulins, albumoses, &c., may be present; but the fluid so obtained, although it may contain all the salts and some of the peptones of the blood, does not resemble it in any other respect, and therefore cannot be taken as affording anything like a natural experiment. Moreover the proof that is offered that these fluids must have extraordinary powers of destroying protoplasm is absolutely inadequate. It is maintained by Hoffmeister that a very considerable quantity of peptone may be obtained from any aggregation of leucocytes, and that even in an abscess a considerable proportion of the peptone is derived from the substance of the leucocytes themselves. A piece of spleen taken from an anthrax animal and introduced into a quantity of this fluid is in the course of eight or ten days found to be in a condition which may be described as coagulative necrosis, and it is assumed that this has been brought about by the action of the lymph fluid. The action of the enormous number of leucocytes in the spleen which will be similar to that in the dying tissues of an abscess is entirely ignored, whilst the peptonising power, which all who have watched the growth of the *Bacillus anthracis* in gelatine know to be present in this organism, is completely left out of account. These bacilli growing for this length of time in the spleen placed in the fluid, in the presence of the leucocytes, must peptonise in a certain degree the whole tissues with which they come in contact.

Mr. Adami's objection to our experiments—on the effect of quinine on the development of anthrax in rabbits—I should be very glad indeed to accept, but to my mind there are two difficulties: on the one hand we have the Scylla, that the quinine breaks down the corpuscles, and if this material is within the leucocytes—though locked up in them and unable to act in the normal condition—it should be set free when the leucocytes are broken down by the quinine, and the anthrax bacilli should be killed;

whilst, on the other hand, if it is set free only in the presence of the products of these bacteria, it should, as Dr. Wood points out, be sufficient to kill the bacilli when introduced into the body in large numbers; the more bacilli present, the greater should be the liberation of the poison from the breaking-down corpuscles, and the greater, therefore, should be the mortality amongst the anthrax bacilli. As a matter of fact this is not the case, though, as Schmidt and his pupils, Buchner, Wright, and others, have pointed out, the leucocytes in the circulation may be enormously increased in number under certain well-known conditions. It is the great objection to Christmas's explanation (published in 1887) of the action of the breaking down of leucocytes in abscesses, in which practically the same theory is put forward, though I scarcely think that it can be said to have been proved. Mr. Adami asks for the conditions under which the experiments, as regards cultivation of anthrax bacilli on an extract of leucocytes, had been made. In talking over the matter with Dr. Wright I find that I had somewhat misunderstood the nature of his experiments, and that he had only grown the *Bacillus anthracis* on extracts of bulls' testicles—in fact, on Wooldridge's tissue-fibrinogen, which, he considered, contained the substances possessing the bactericidal powers of the extract of the thymus. It might, therefore, be objected that this experiment was not by any means crucial, and I therefore asked Dr. Wright to repeat his experiments on some tissue known to contain a large number of leucocytes. He has, therefore, during the last fortnight made an extract of the thymus gland pounded up in salt solution, in order to obtain a solution of nucleo-albumen, of globulin, and other albumens. This was carefully filtered through a Chamberland's filter, incubated for a short time in order to determine whether it was free of germs or not, and then inoculated with anthrax. If this bactericidal material, so potent but so subtle, were present in these dead leucocytes, there should be no growth of these organisms in this fluid. They were thoroughly shaken and then incubated, with the result that in every case there was multiplication of the organisms, very pure cultures being obtained; so far from losing their virulence, they were proved by Dr. Wright to be capable of killing guinea-pigs in practically the same time as the control anthrax. The composition of these fluids I shall leave the physiological chemists to determine amongst themselves; but there seems to me to be little doubt that many of them are working at

the same substance under different names, and it is my firm conviction that in the many experiments in which bactericidal power has been noted in fluids this result has been due to the fact that wherever it has occurred there has been a rapid breaking down of unstable proteids and a setting free of certain molecules which in their nascent condition have the power of combining with the protoplasm of micro-organisms, and of thus rendering such micro-organisms inert or incapable of continuing their functional and vegetative activities.

In the work of scavenging and even of taking up living vegetable protoplasm, however, I look upon the living leucocyte as being worth more than two dead ones, and in the light of the positive evidence we have of phagocytosis, and of the absolute impossibility of obtaining any evidence of the bactericidal activity of the fluid constituents of the blood in the body apart from the living cells, I am still of the opinion that phagocytosis is a more potent factor in the production of immunity and in the protection of an animal against the attacks of micro-organisms than are these fluid constituents. Naturally, until we understand the origin of leucocytes more thoroughly and the developmental cycle of the so-called fixed cells, we shall not be justified in accepting the theory of phagocytosis as the ultimate explanation of immunity. It is possible—nay, I think it is almost proved—that the fixed tissue-cells play an important part in coming to the aid of the leucocytes, and, as in inflammatory processes, it is probable that the leucocytes act the part of light cavalry (to use a well-worn simile), whose duty it is to keep in check the invader until the main body of proliferating connective-tissue or fixed cells can come up to capture or repel the invading forces, or until they can be accustomed to the new sets of conditions in which they find themselves; but all these, whether leucocytes or connective-tissue cells, may become so modified after contending with different forces, that should they resist a first attack they are enabled in their inured condition and by the special modification of their protoplasm to repel much more readily any second attack.

It may be that more attention has hitherto been directed to the leucocytes as phagocytes than to connective-tissue cells, from the fact that, owing to their greater powers of motion, and to the readiness with which they may be isolated and examined, any alterations in their protoplasm have a much greater effect in

modifying their demonstrable behaviour. These very characters, however, might suggest the probability that they do actually play a more important part in the destruction and removal of foreign bodies than the fixed cells, which may become modified not only in outward form, but also in character, before we are able to observe any change of function within them. It must be maintained, however, seeing that the sources of leucocytes and of the fixed cells cannot be very unlike, that any modification of protoplasm through the action of chemical products introduced into the circulation as the result of the vital activity of bacteria, must occur in leucocytes and fixed connective-tissue cells alike; and although the evident results may be different, it must be accepted that they are to a common end. It may be that the leucocytes do the scavenging in the first instance, where the processes are acute, and where it is necessary that the removal of foreign material should go on radidly, the fixed connective-tissue cells being called in to help at a later stage, in some cases merely to remove the *débris* of their more rapidly acting allies. In chronic processes the mononucleated macrophages are always far more numerous than in acute conditions.

In addition to the facts already brought forward, I should like to indicate one or two points that have a somewhat important bearing on this controversy of immunity.

1. Chemotaxis is not due to a mere irritant or stimulating action of chemical substances on protoplasm. We have both an attractive and a repellent action, which cannot be due to any difference in the intensity of a stimulus, though we undoubtedly find that the protoplasm of certain cells may become so accustomed to the presence of a poison that ultimately, in place of avoiding, it will attempt to destroy it.

2. Immunity is entirely a relative term, and the clinical immunity that we observe in many patients may only be efficacious if the disease is conveyed by what we may speak of as *natural channels;* such clinical immunity being much more easily obtained than our experimental immunity, which, though much more complete, is still only relative, as it appears to be almost impossible to produce a condition of absolute immunity against any disease.

3. The serum of rats, according to Hankin, kills the *Bacillus anthracis*, but these animals are by no means immune to anthrax, so that we have in the serum in its altered condition, and when

separated from the blood (and therefore acting as a dead proteid, having a different and probably a rapidly altering chemical composition), a substance which will insure the destruction of the *Bacillus anthracis*, whilst the fluid elements of the *living* blood appear to exert comparatively little influence on these same bacteria. Similarly the *Vibrio Metschnikovi* is easily destroyed by the serum of vaccinated guinea-pigs when these are placed together in a test-tube, but the same organism may still continue to grow in the fluids in the body of a living vaccinated animal, the death of which, however, it is then not able to determine; whilst after growing in such a living animal body it appears to be able to grow even when transferred to a test-tube containing separated serum, so that it would appear that we have an acclimatisation of the bacillus just as we may have an acclimatisation of the cells. It is possible, too, that the inflammatory serum met with in certain diseases may, as the result of the unstable condition of its proteids, exert not only an attenuating, but even a definite bactericidal power on certain micro-organisms within the body. It has been claimed that the serum may destroy the poison, and not the bacilli which form such poison; but such antitoxic action is exceedingly transitory, and although it may play a part in the production of immunity, we have, as yet, neither definite nor satisfactory evidence in support of it. Even in cases where no antitoxic action of the serum can be demonstrated, and where the serum itself has no power of destroying the bacilli, the poisonous products when administered in minute doses to an animal will often induce a very considerable degree of protection against the disease associated with that poison, and with the organisms that produce it; and from what has above been stated it is, we may assume, clear that this protection is due to the action of the poison on the tissues, which are so altered that they are able to carry on successful combat with the micro-organisms that are afterwards introduced.

These, gentlemen, are some of the points that will have to be dealt with in working out this very difficult question; on some of them I should like to have given a more detailed and definite opinion, but our time is limited, and our President will touch more or less fully on the more important questions that have been raised in this discussion—questions which it will be the duty of those engaged in clinical and in laboratory work to pursue to a more definite conclusion.

The PRESIDENT, having thanked those who had contributed to the discussion, congratulated England on its rising school of bacteriologists, who had accomplished so much, though having great disadvantages to contend against owing to the false sentimentalism and prejudices against the true interests of humanity which existed in this country. Though he expressed himself as unable to sum up at all adequately the points of the discussion, yet he desired to offer the impressions the remarks of the speakers had made on his own mind. Zymotic diseases were dependent upon the introduction of micro-organisms into the system, and these microbes possessed the power of rapid propagation, and exerted a pernicious effect upon the organs of the body. They produced, moreover, certain excreta or toxines, which, even more than the microbes themselves, were prejudicial. The microbes and their toxines could not be dissociated; they both came into contact with the cells of the body and with the body fluids. These body cells were undergoing continual change—change essential to their vitality, absorbing, modifying the material absorbed, and returning what was excreted into the fluids around. All body cells were phagocytes; that was an essential feature of their existence. But they were promiscuous feeders, and would take up other things besides those normally supplied from the blood—they would absorb foreign matters—they would certainly absorb bacteria. Speaking technically, they were phagocytic as regarded the bacteria with which they came in contact, and there was abundant microscopical evidence of this, that they could exercise a solvent or destructive influence upon them. By far the majority maintained that the cells were an important element in the destruction of bacteria. Professor Burdon-Sanderson had found it difficult to conceive that there could be any special function in cells by which they could exert this malignant influence upon bacteria. But it was not necessary to assume that they were specially bactericidal; they were only phagocytic to bacteria by virtue of their general phagocytic qualities; it was a part of their general natural function, and not a special endowment. There was evidence that certain poisonous elements introduced into the blood did tend to attract leucocytes into their neighbourhood. In some cases the cells, so attracted, overpowered and destroyed the bacilli; while in other cases they failed to do so, and the microbes spread over the system. In such instances cells might be found packed with

microbes, the latter afflicting the former with such an indigestion as to cause their death. On the whole, the general result of the discussion seemed to be in favour of the phagocytic action of leucocytes and other cells upon bacteria. A much more difficult question was the effect of the body fluids upon the bacilli and their toxines. In considering that, we passed out of the range of ocular inspection, and almost beyond the range of chemical examination; we had to deal with fluids of very peculiar composition and very great instability. It was found that the fluid serum in the test-tube might be fatal to a micro-organism; and yet, inject that microbe into an animal from which the serum was obtained, and it would flourish there. This showed with what delicate materials one had to deal. In this part of the discussion it seemed to him that the probability was in favour of the humoralistic view. But the fluids and the solids of the body interacted so intimately each upon the other that there could be no such thing as solidism and humoralism separately. Anything that could affect the blood-serum must also produce an effect upon the cells and the bacteria in it. The toxine of the bacteria diffused throughout the blood-serum must exert some pernicious effect upon that serum as well as on the cells, and the serum so altered might finally react on the bacteria, and we must not assume that there was no effect because we could not demonstrate it. All the results he had spoken of so far had been obtained by experiment upon animals, but Dr. Bristowe had thrown some practical light upon the subject. He had remarked especially upon the resistance offered to the entrance of bacteria to the body, and referred to the probability that they became altered in their passage. When we considered the utterly inappreciable evidences there were to account for the degree of immunity possessed by different persons, we should not be surprised that it was surpassingly difficult to trace out the causes of immunity in different animals. He regarded it as almost hopeless to form an idea of the essential nature of the change which produced immunity from small-pox by vaccination. He regretted that the point of exhaustion had been rather summarily excluded from the debate. The manner in which a disease attacked one part, ceased there, and passed to another was difficult to explain on any view, phagocytic or other. The migration area in the course of a common cold was an instance in point. He referred to the phenomena of scarlatina, its incubation, its sudden accession, the sequence of phenomena to

quiet subsidence, and, if not fatal, the immunity of the subject for a period. How was this explained by phagocytosis or any other theory? To what influence did the microbes succumb after having obtained a maximum of power? Was it because of some poison which they themselves engendered, or because they had exhausted the pabulum upon which they existed? It was difficult to explain the course of certain diseases of the skin by any theory of phagocytosis. We might rest assured that the interest in this subject had not yet passed away, for many of these problems were still invested with uncertainty, and that uncertainty was an invitation to work yet to be done.

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